

CYCLISATION REACTIONS OF DIAZOALKENES

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I declare that I have attended the following lectures, etc., during the course of this research.

Recent Developments in the Theory of Concerted Processes,

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Organometallic Processes in Organic Chemistry,

by Prof. P.L. Pauson.

Industrial Research and Development,

by Dr. B. Gravenor.

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ABSTRACT

This Thesis is concerned with the reactions of $\alpha\beta$ -unsaturated diazoalkenes, including such compounds which also have $\gamma\delta$ -unsaturation as part of an aryl ring. These diazoalkenes are produced in aprotic solvent by the thermal decomposition of tosylhydrazone sodium salts. The effect on these reactions, notably cyclisations, of steric constraints and of substituents has been examined.

The research uncovered examples of diazoalkenes which decompose via carbenes to give hydrocarbons, and others which react with retention of nitrogen to give 1,2-benzodiazepines and 3H-pyrazoles. The novel expansion of a 3H-pyrazole to give a diazepine is described, as are certain thermal and acid-catalysed rearrangement reactions of 3H-pyrazoles.

Reaction mechanisms, based on the evidence of both the literature and this research, are discussed.

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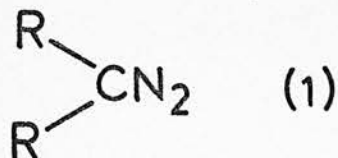
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INTRODUCTION

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FORMATION AND REACTIONS OF DIAZO-COMPOUNDS¹

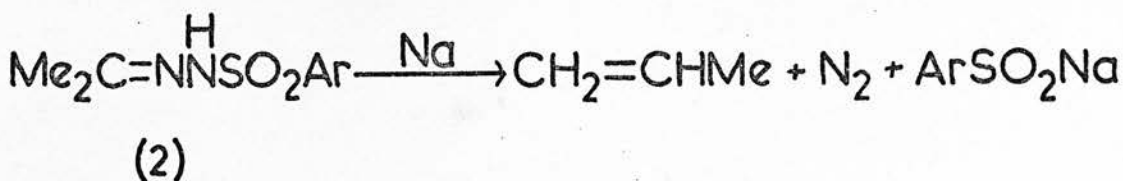
Diazo-compounds (1) are unstable species which can react in a number



of ways. They are readily protonated to give diazonium salts and thence carbonium ions, and they are also one of the most important sources of carbenes. Diazo-compounds can react as 1,3-dipoles and this makes them useful in the preparation of such heterocyclic systems as pyrazoles, pyrazolines and diazepines. The physical and chemical properties of diazo-compounds will now be discussed.

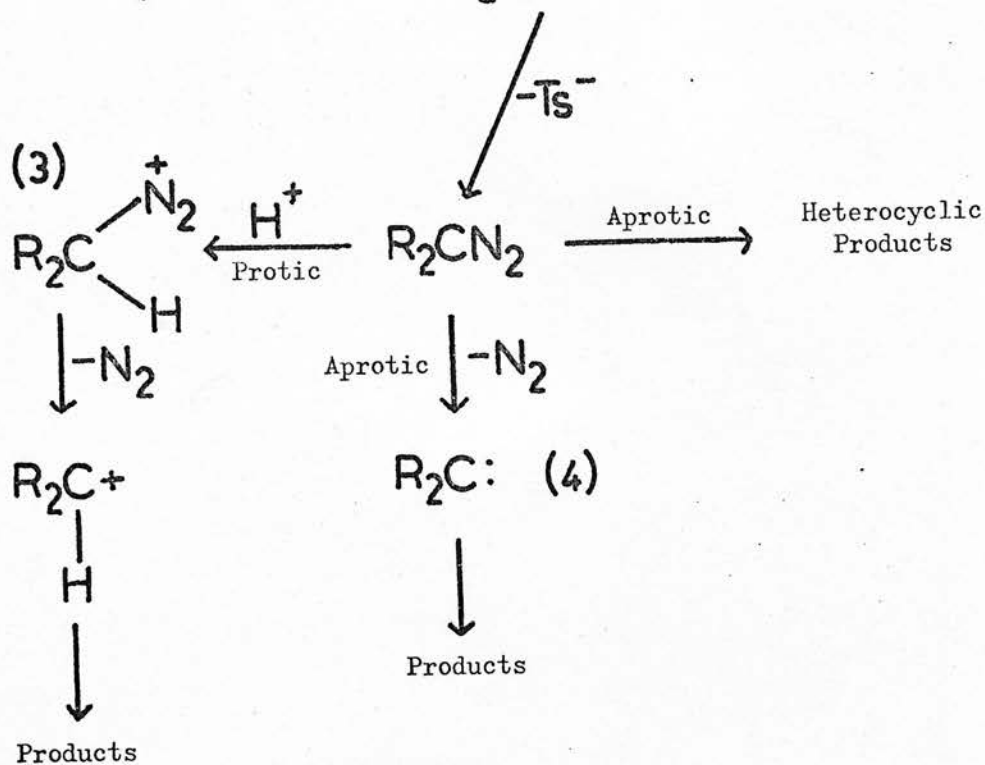
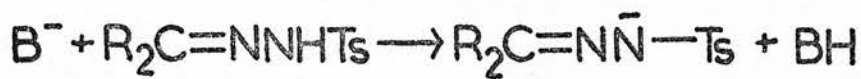
1. Methods of Formation

One of the most widely used methods of preparation of diazoalkanes, and the method which was used in this research is the base-induced decomposition of tosylhydrazones. Bamford and Stevens² in 1952 were the first workers to carry out this decomposition. They found that olefins were formed when aliphatic tosylhydrazones (2) were heated in ethylene glycol with sodium.

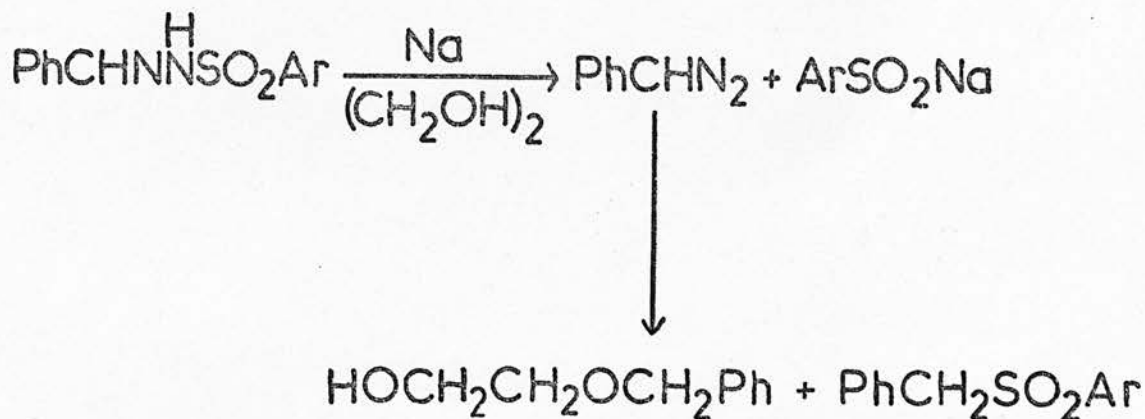


Tosylhydrazones of aromatic aldehydes and ketones decomposed under the same conditions to give products which were the same as those formed from the corresponding diazo-compound. This led Bamford and Stevens to conclude that diazo-compounds were intermediates in the decomposition.

The mechanism of the decomposition has been intensively studied, and



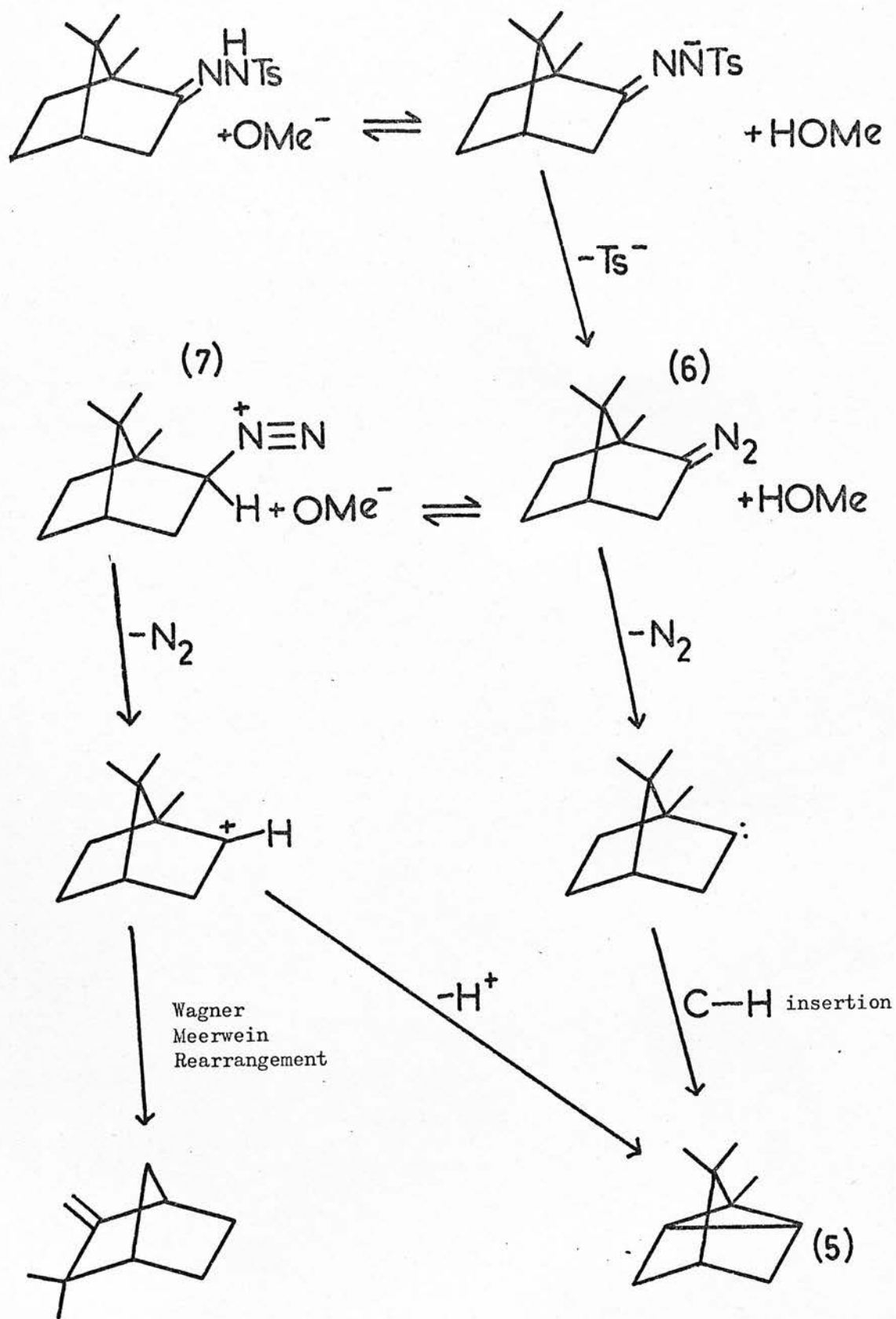
Scheme 1



has been shown to depend on a large number of factors,³ including the ability of the solvent to donate and accept protons, the type and concentration of the base, the presence of metal cations and Lewis acids, the polarity of the reaction solvent and the structural constraints on the substrate. In many of the early mechanistic investigations, the workers failed to appreciate the number of variables involved, and some of their conclusions must be considered with this in mind.

Through the work of Bamford and Stevens,² Heubaum and Noyes,⁴ and Powell and Whiting,⁵ it has become accepted that the mechanism of the base-induced decomposition of tosylhydrazones is that shown in scheme 1. After loss of the *p*-toluenesulphinate anion, the diazo-compound can be protonated by a suitable solvent to form the diazonium cation (3) which can then lose nitrogen to form the carbonium ion. In aprotic solvents, the diazo-compound will either form heterocyclic compounds by a non-ionic mechanism, or else will eliminate nitrogen to give the carbene (4). It must be stressed, however, that the solvent is only one variable. It is quite possible to have products derived from carbonium ions even in an aprotic solvent if a deficiency of base is present.⁶

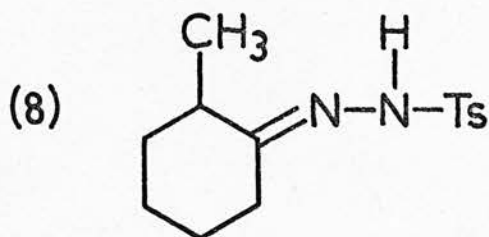
Shapiro and co-workers⁷ have studied the effect of varying the base concentration in the decomposition of camphor tosylhydrazone (scheme 2), while keeping other factors constant. In decalin, diglyme and dimethylformamide they found that increasing the quantity of base (NaH and NaOMe)



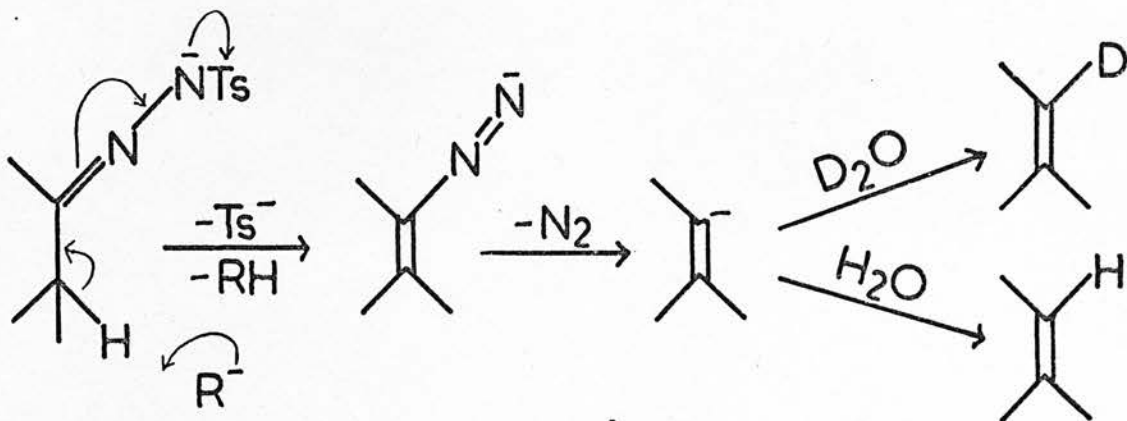
Scheme 2

from 0.25 to 1.5 times the equimolar amount, caused an increase in the proportion of product (tricyclene (5)) derived from the carbene. The proposed mechanism involved an equilibrium between diazocamphane (6) and its diazonium cation (7). Excess base pushes the equilibrium in favour of the diazo-compound and hence favours the formation of tricyclene (5) by a carbenic route. Less than one equivalent of base favours the cation, and hence the formation of products by the carbonium ion route.

An entirely different mechanism, not involving diazo-compounds has been proposed for the reactions of tosylhydrazones, e.g. 2-methylcyclohexanone tosylhydrazone (8) with very strong bases (alkyllithium) at low temperatures



(0-90°).^{8,9} Reactions of this type give good yields of alkenes from tosylhydrazones with α -hydrogen atoms, and are thought to involve carbanion intermediates.

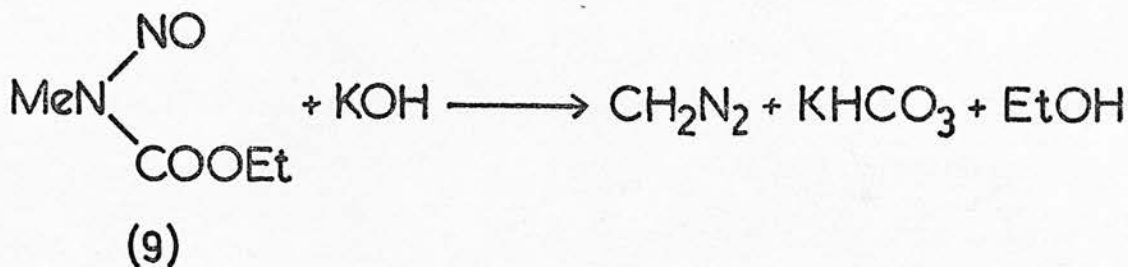


This mechanism is supported by the uptake of deuterium from deuterium oxide.

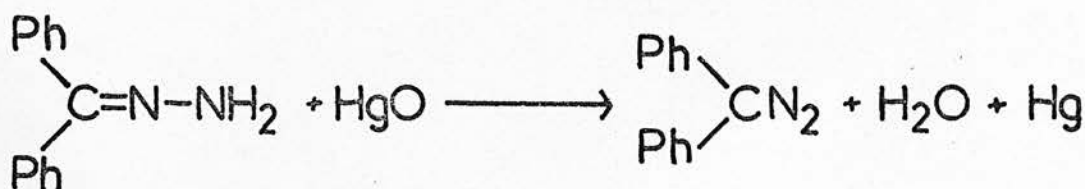
Thus, the conditions of tosylhydrazone decompositions can be chosen

such that the products will be derived from carbenes, carbonium ions or carbanions.

The classical preparation of the simplest diazoalkane, diazomethane, is the treatment of an N-nitroso-compound, e.g. N-nitroso-N-methylethylurethane¹⁰ (9) with base.

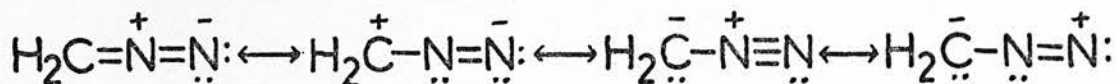


Disubstituted diazo-compounds can be prepared by the oxidation of ketone hydrazones.¹¹



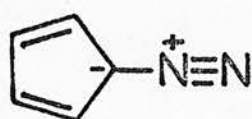
2. Stability and Structure

The simplest diazoalkane is diazomethane. It is highly unstable, toxic and hence difficult to work with. Its structure can be represented as a resonance hybrid of the canonical forms shown below.

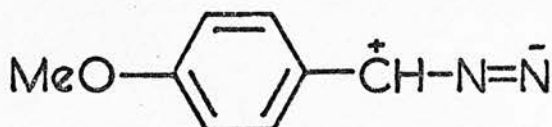


Firl and co-workers,¹² have used ¹³Cn.m.r. spectroscopy to show that the carbon in diazomethane has a high electron density ($\delta 23.1$), showing that there is a large contribution from the structures with a negative charge on the carbon.

The stability of larger diazo-compounds depends on the nature of the substituents on the diazo-carbon. Conjugating substituents always increase the stability regardless of whether they are electron releasing or withdrawing. Non-conjugating electron withdrawing substituents favour the structures having a formal carbanion ($R_2\bar{C}-N_2^+$), whereas electron releasing substituents favour a formal positive charge on the carbon atom ($R_2\overset{+}{C}-N_2^-$). Diazocyclopentadiene (10) is an example of the former and *p*-methoxyphenyl diazomethane (11) is an example of the latter.



(10)

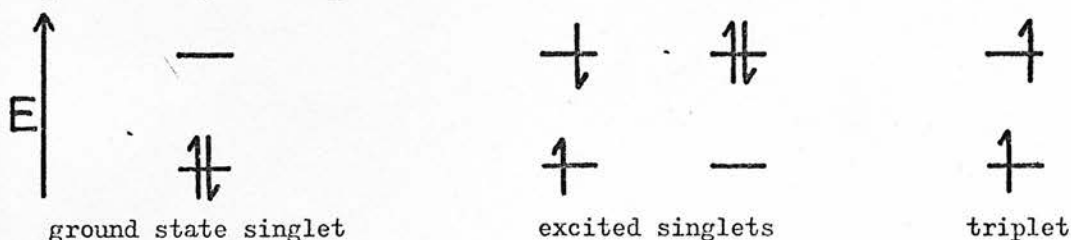


(11)

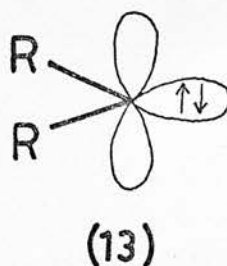
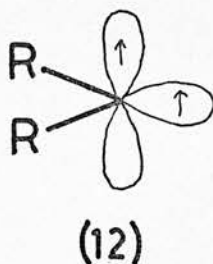
Non-conjugating substituents on the diazo-carbon increase the stability of the diazoalkane if they are electron withdrawing, but decrease the stability if they are electron donating.¹³

3. Carbene Formation and General Reactions of Carbenes^{14,15}

The photolysis or thermolysis of diazoalkenes in aprotic solvents provides the most common general route to carbenes. The two non-bonding electrons of a carbene may have parallel spins (triplet state) or anti-parallel spins (singlet state).

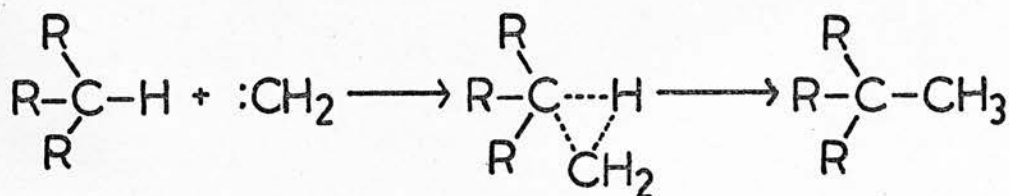


Most carbenes have a bent triplet ground state (12), but some, e.g. halocarbenes, have singlet ground states (13).

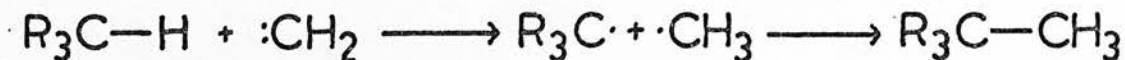


Carbenes can undergo any or all of the following reactions: insertion, addition, rearrangement, and reaction with their diazoalkane precursor to give an azine.

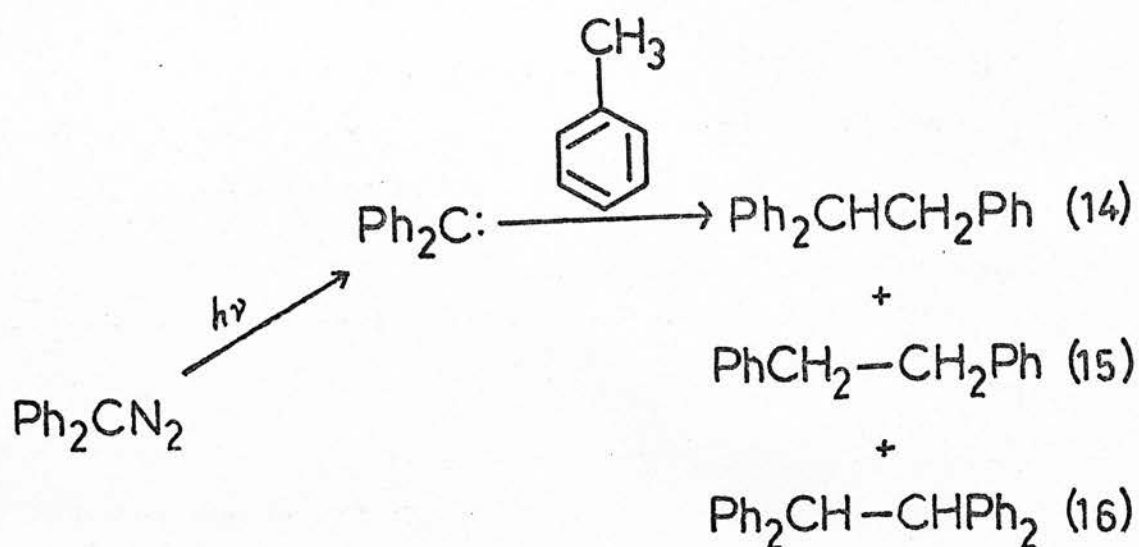
Insertion reactions of carbenes, most commonly into C-H bonds, can be stereospecific or non-stereospecific, corresponding to the concerted¹⁶ and non-concerted¹⁷ mechanisms respectively. The concerted process involves a three-centre transition state.



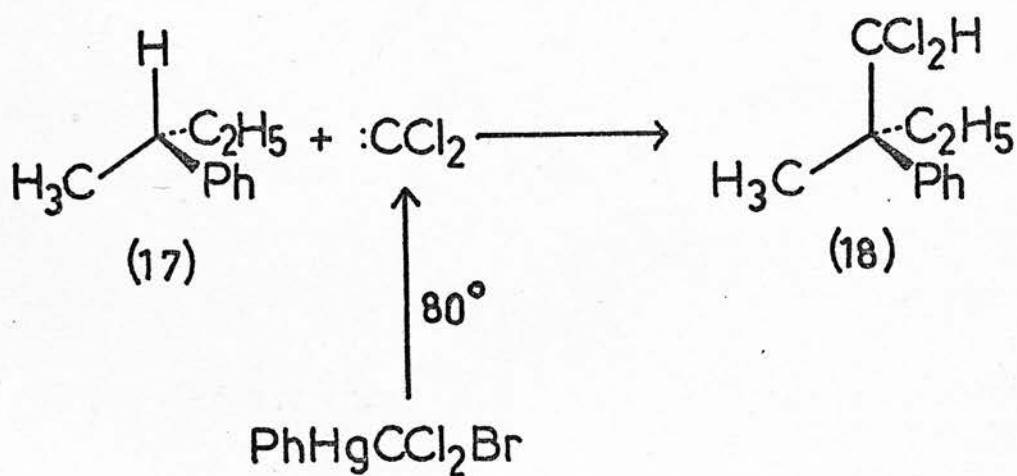
The configuration of the substrate is retained in the product if this mechanism operates. The non-concerted alternative is an abstraction-recombination process.



Since this method involves radicals, the configuration of the substrate will presumably be lost and this provides a good test of the mechanism. We



Scheme 3



Scheme 4

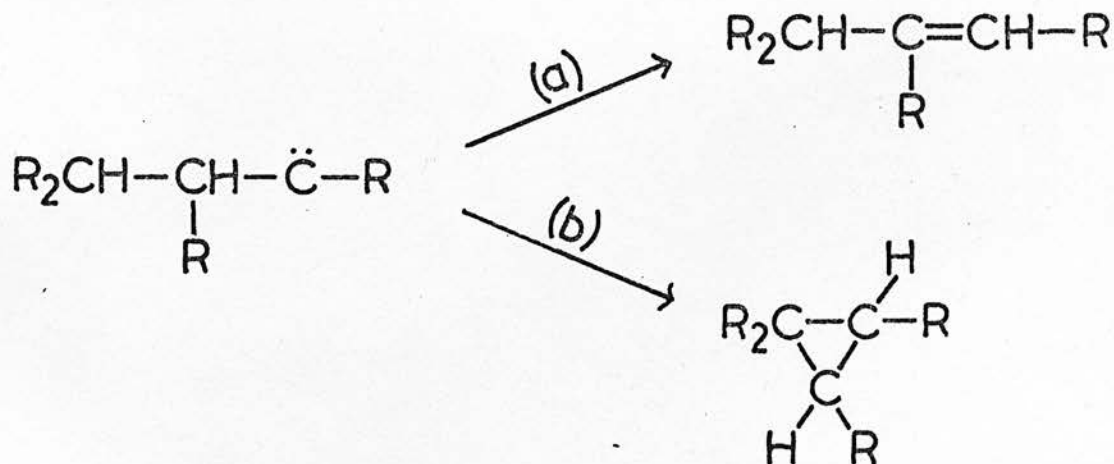
might also predict other products from the intermediate radicals formed by rearrangement, abstraction, and dimerisation, as well as the recombination product, although the recombination could still be very efficient if the radicals were held close together, in a solvent cage. There is experimental support for both mechanisms, and it appears that there is a correlation between the mechanism, and the multiplicity of the carbene.

Diphenylcarbene, which has a triplet ground state has been shown to insert by an abstraction-recombination mechanism (Scheme 3).¹⁸ As well as the insertion product (14), the two other radical recombination products (15,16) are found. A chemically induced dynamic nuclear polarisation (CIDNP) study of this system¹⁹ has shown that the three products are formed from radicals.

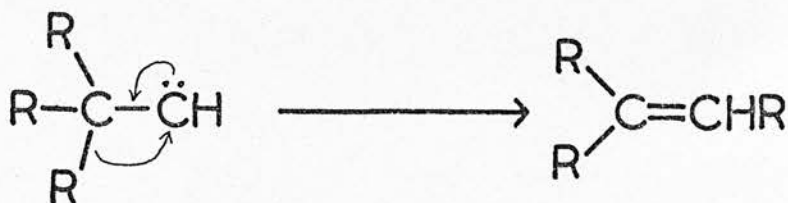
Conversely, dichlorocarbene, a singlet, has been shown to insert in a concerted manner (Scheme 4).²⁰ Optically active 2-phenylbutane (17) reacted stereospecifically with dichlorocarbene to give optically active 1,1-dichloro-2-methyl-2-phenylbutane (18).

Two important types of intramolecular carbene insertions are:

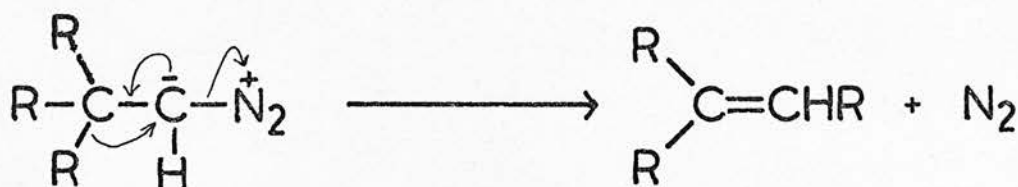
(a) into an α -carbon-hydrogen bond to form an olefin, and (b) into a β -carbon-hydrogen bond to form a cyclopropane.



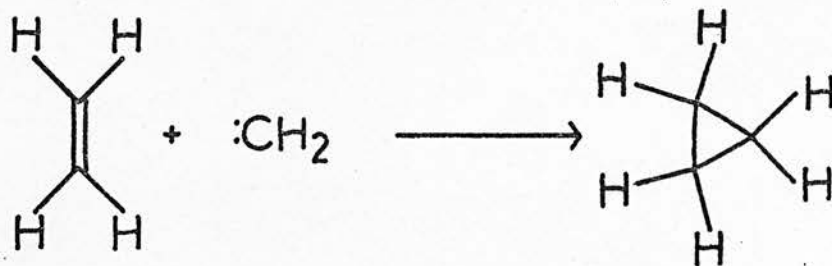
As well as 1,2-hydrogen shifts as in (a), other groups, e.g. alkyl, aryl, alkoxy, can undergo such shifts.



However, it is often difficult to distinguish between the above mechanism and one involving concerted migration of the group R and expulsion of the leaving group.

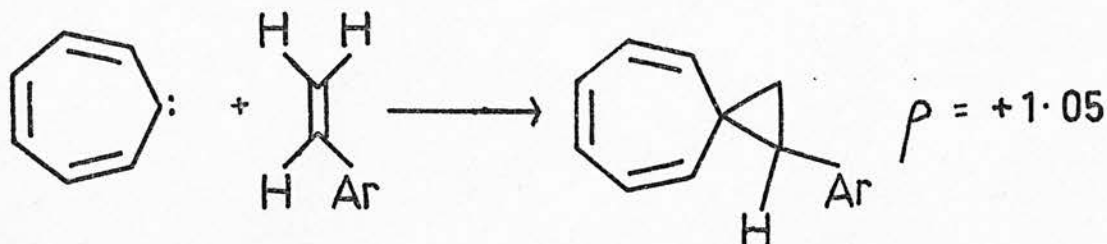


One of the most characteristic reactions of carbenes is their addition to olefins to give cyclopropanes.



Skell and Garner²¹ and later Hoffmann²² showed on theoretical grounds that the ground state singlet adds stereospecifically, whereas triplet or excited state singlet carbenes add non-stereospecifically. Skell describes this phenomenon in terms of spin states, whereas Hoffmann uses the concept of spatial distribution of the wave function. Thus, the correlation between multiplicity and stereospecificity is shown to hold for both insertion and addition reactions of carbenes.

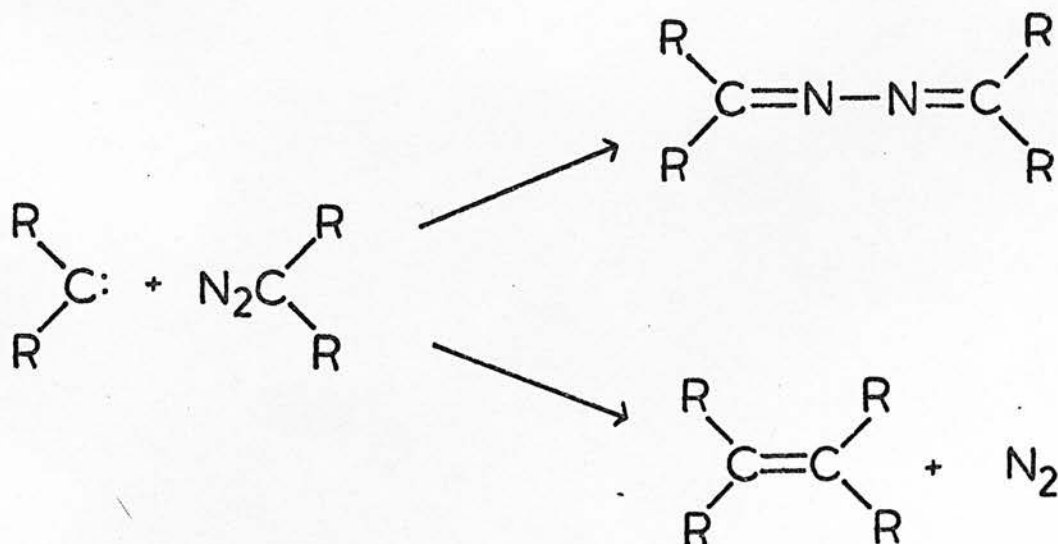
Most carbenes are electrophilic in character, and add readily to double bonds, however it has recently been shown²³ that some carbenes are nucleophilic.



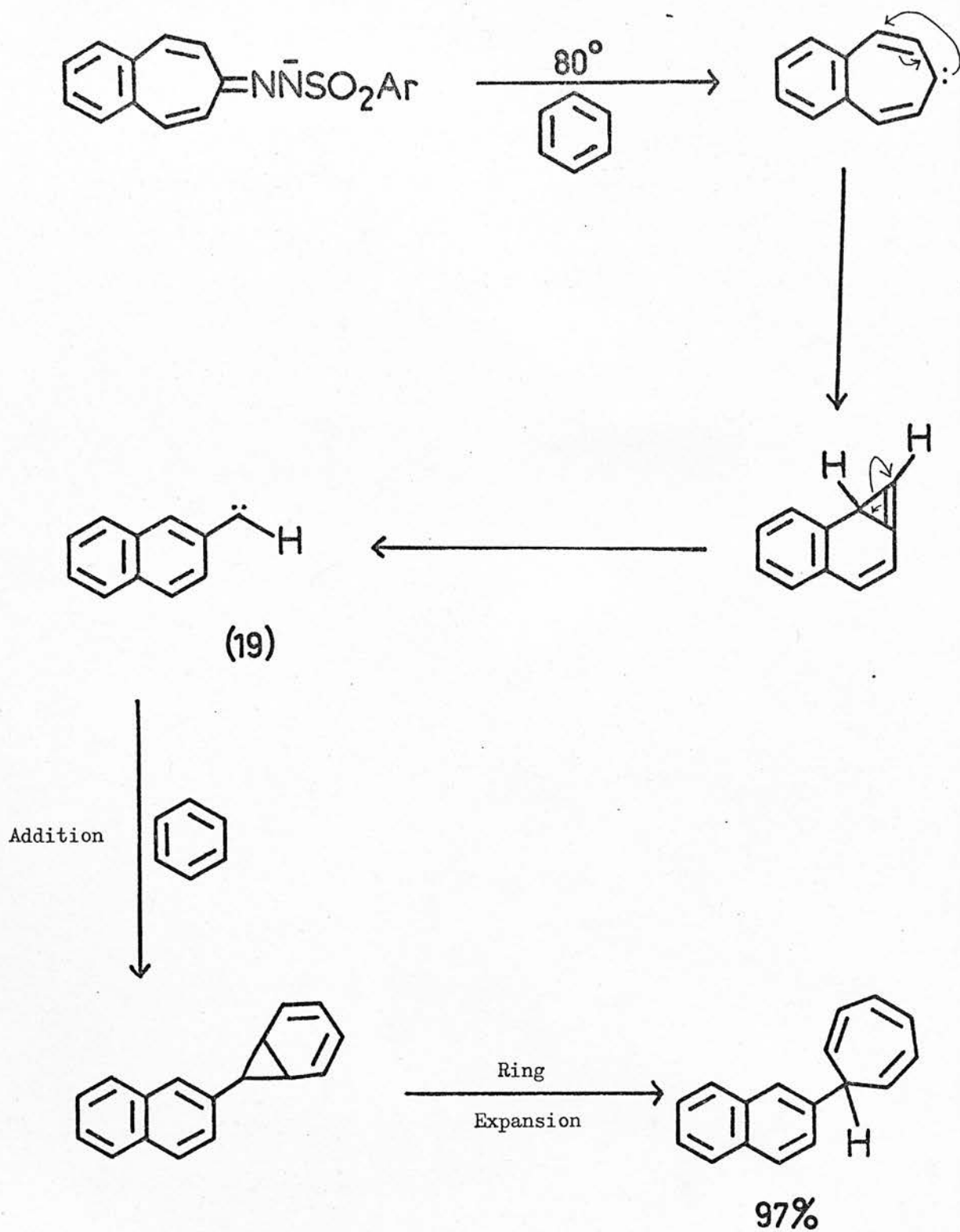
The reason for this unusual feature is that nucleophilic carbenes are most stable if the two carbene electrons are in the sp^2 orbital in the plane of the molecule. This allows $4n + 2$ π -electrons to give the molecule aromatic stability. The vacant p-orbital on the carbene is a poor electrophile as such a reaction would upset the π -system.

Carbenes can also add to allenes, alkynes and aromatic compounds.

Carbenes are such short-lived intermediates that their dimerisation is unlikely. A common reaction, however, is attack on the diazoalkane precursor to give either the azine or the apparent "dimer".



Of the large number of rearrangements which carbenes are known to undergo, those which are of most relevance to this work are the recent



Scheme 5

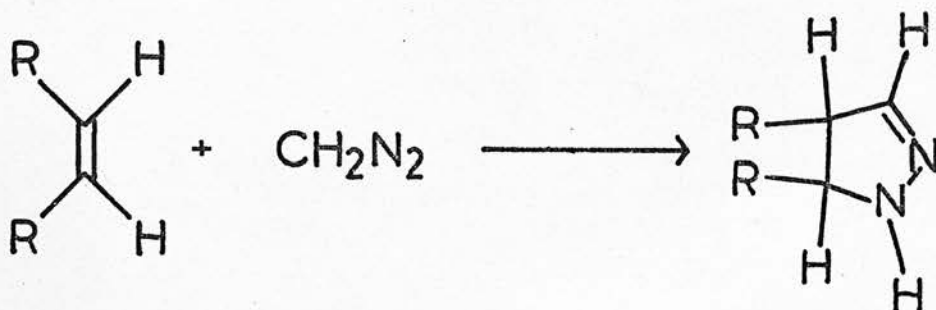
developments in carbene-carbene rearrangements in aprotic solvents, carried out by Jones and co-workers.^{24,25} (Scheme 5)

The β -naphthyl carbene (19) can also be detected by its insertion into cyclohexane and diglyme. Wentrup²⁶ has recently carried out thermochemical calculations which have given a unifying explanation of the majority of the experimental data published to date.

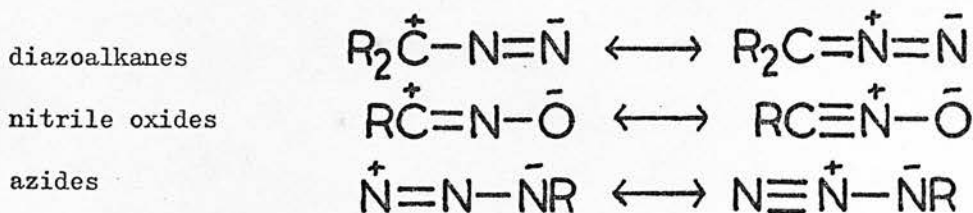
4. Electrocyclic Reactions

(a) Intermolecular Cycloaddition Reactions

Cycloadducts of diazoalkanes have been known for a great many years. For example, in 1910 Oliveri-Mandala²⁷ synthesised pyrazolines using diazomethane.



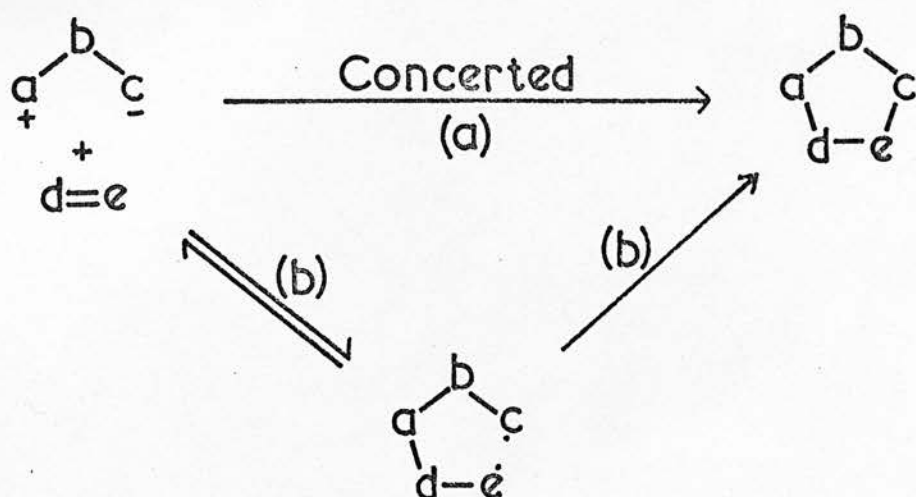
In the early 1960's, diazoalkanes were shown by Huisgen^{28,29,30} to be members of the class of 1,3-dipolar molecules which undergo 1,3-cycloadditions, and are described by the zwitterionic structures shown below, e.g.



1,3-Dipolar cycloadditions exhibit common mechanistic features: they are not markedly influenced as to rate or stereochemistry by solvent polarity; they show low enthalpies of activation, and large negative entropies of activation; they produce five-membered cyclic compounds in which the stereo-

chemistry of the reacting olefin (dipolarophile) is maintained. The reaction rates are markedly increased by conjugation of the reacting site in the olefin, but reduced by the steric effect of all types of substituent. Reactivity of diazoalkanes in cycloaddition is markedly reduced by conjugating substituents on the diazo-carbon, but is increased by alkyl groups. This is in line with the stabilities of these two types of diazo-compounds.

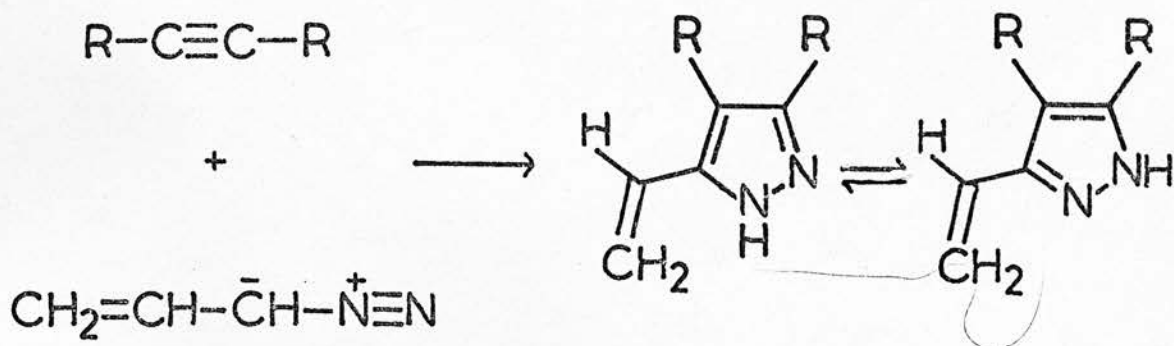
The mechanism of cycloaddition has come under intense investigation. Basically, the problem has been to decide between a concerted and a two-step mechanism.



Firestone^{31,32} has recently argued in favour of a non-concerted mechanism involving radicals (route b). Huisgen,²⁸ however, had previously proposed that 3 + 2 → 5 cycloadditions occurred via a concerted process (route a) involving a cyclic transition state. Firestone claims that the unidirectionality of orientation exhibited by most 1,3-dipoles towards both electron rich and electron poor dipolarophiles supports the diradical mechanism as one of the possible diradicals would be more stable than the other. He also claims that steric effects and the fact that there is only a small solvent effect supports his mechanism. Huisgen,^{28,30} however, claims that the cis-stereospecificity of the cycloaddition, together with activation parameters support the concerted pathway. He also says that the magnitude of the

solvent effect is entirely adequate for the concerted pathway. Woodward and Hoffmann³³ have shown that Huisgen's mechanism is allowed, in a supra-supra sense, by orbital symmetry. The matter is as yet unresolved.

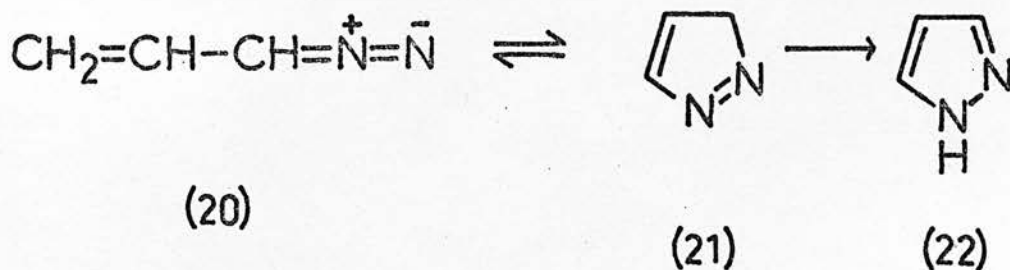
Unsaturated diazo-compounds may react with dipolarophiles to give pyrazolines and pyrazoles in the normal manner.³⁴



They may also undergo an intramolecular cycloaddition yielding pyrazoles.

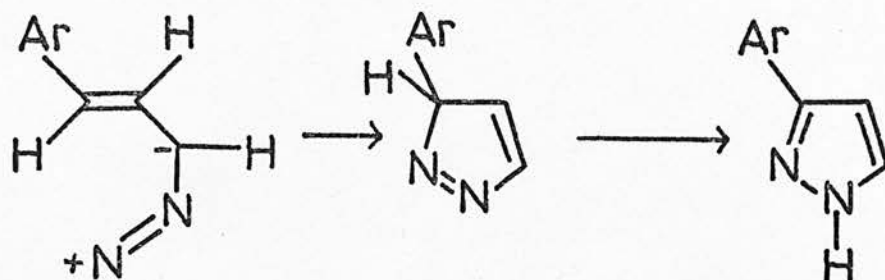
(b) Intramolecular Cycloaddition Reactions

In 1935^{35,36} 3-diazopropene (20) was shown to spontaneously cyclise to pyrazole (22).

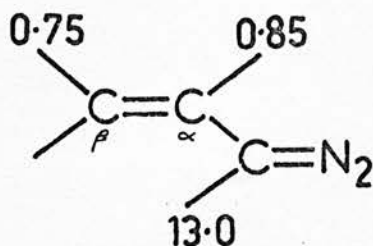


In 1967, Ledwith and Parry³⁷ reinvestigated this reaction and reported that the rate of reaction was enhanced by light. They postulated the 3H-pyrazole (21) as the absorbing species in the reaction, as 1,3-dipolar cycloadditions of diazoalkanes are not accelerated by light.

The mechanism of these intramolecular cycloadditions has been investigated by Brewbaker and Hart,¹³ who studied a series of aryl and alkyl substituted diazoalkenes. They allowed these compounds to slowly cyclise in cyclohexene at room temperature, and obtained good yields of 1H-pyrazoles.

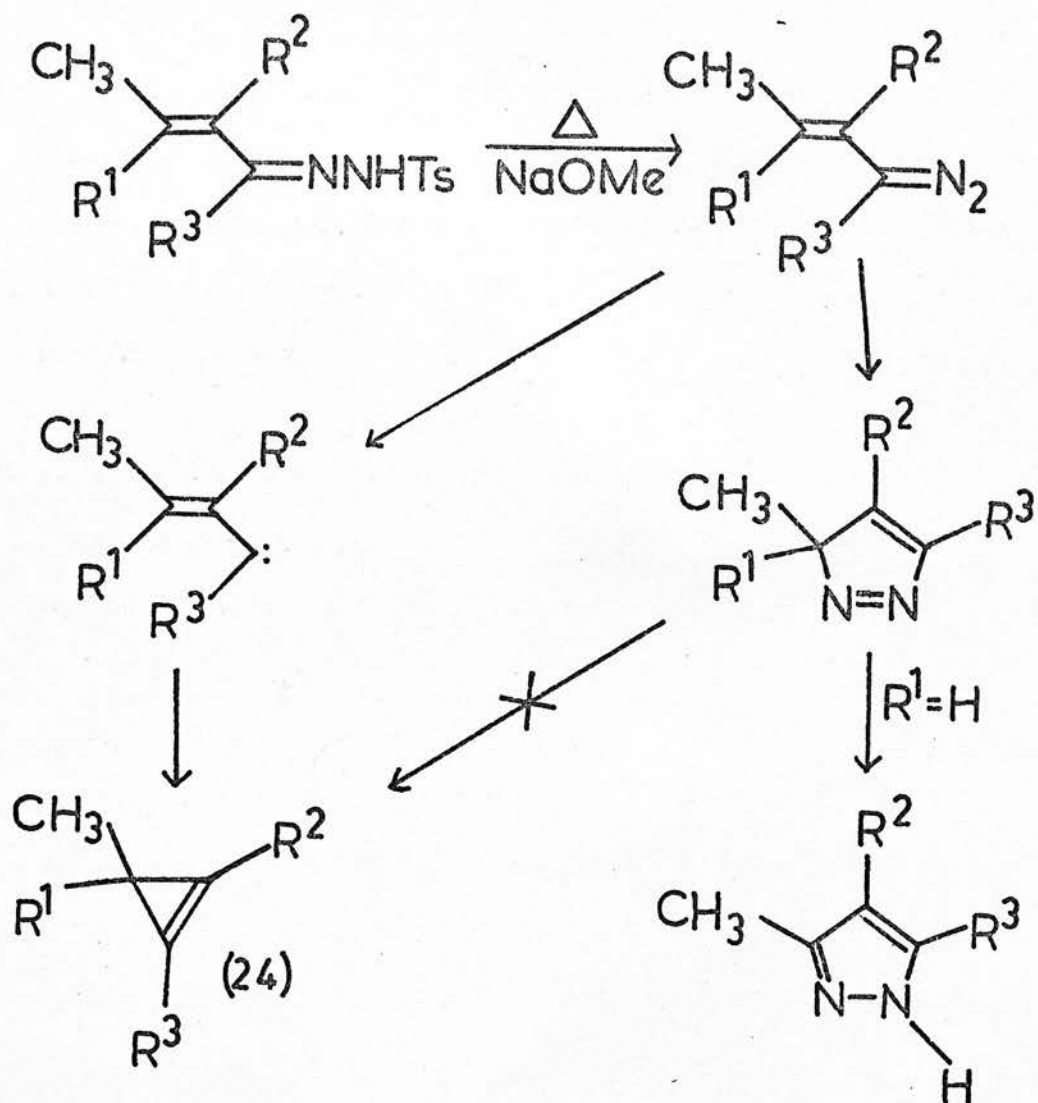


It was found that a conjugating aryl substituent on the β -carbon of the diazoalkene increased the rate of cyclisation to the pyrazole, but substitution of electron withdrawing and electron releasing substituents in the phenyl ring had little effect on the rate. Methyl substituents on the α and β -carbons of the diazoalkene slightly reduce the rate of cyclisation of 3-diazopropene, whereas methyl substitution on the diazo-carbon has a marked accelerating effect. The relative rates of cyclisation of the three methyl substituted 3-diazopropenes, as compared to the parent compound are shown below.



The marked accelerating effect of the methyl group on the diazo-carbon is probably due to the electron releasing property of the group causing reduced stability.

All these results support the conclusion that cyclisation of 3-diazoalkenes to pyrazoles is an intramolecular, concerted, 1,3-dipolar cyclo-



Scheme 6

| Compound | R^1 | R^2 | R^3 | Yield (24) % |
|----------|-------|-------|-------|--------------|
| A | Me | Me | H | 72 |
| B | Me | H | Me | 39 |
| C | Me | H | H | 50 |
| D | H | Me | H | 4 |
| E | H | Me | Me | 1.5 |
| F | H | H | H | 3 |

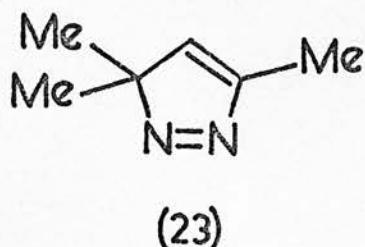
Table 1

addition.

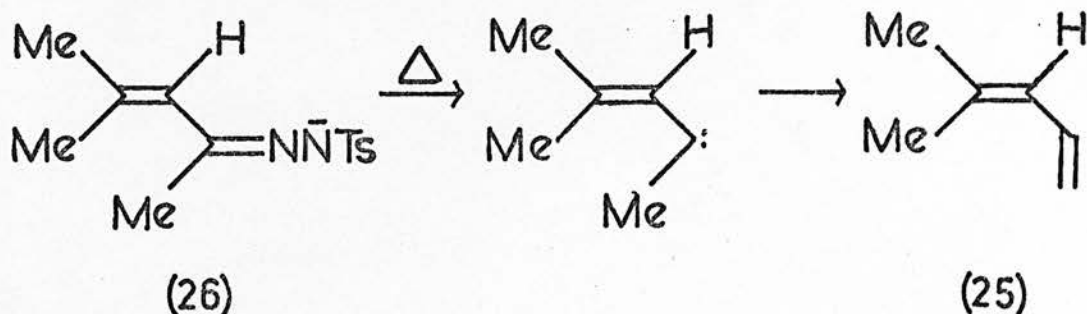
The first report of the decomposition of the sodium salt of unsaturated tosylhydrazones was that of Closs and co-workers.³⁸ Under conditions of a 2 to 2.5 fold excess of sodium methoxide over tosylhydrazone in aprotic solvent (diglyme or diethyl carbitol) at 160–220°, these workers formed cyclopropenes and pyrazoles (Scheme 6). Cyclopropene yields are given in Table 1.

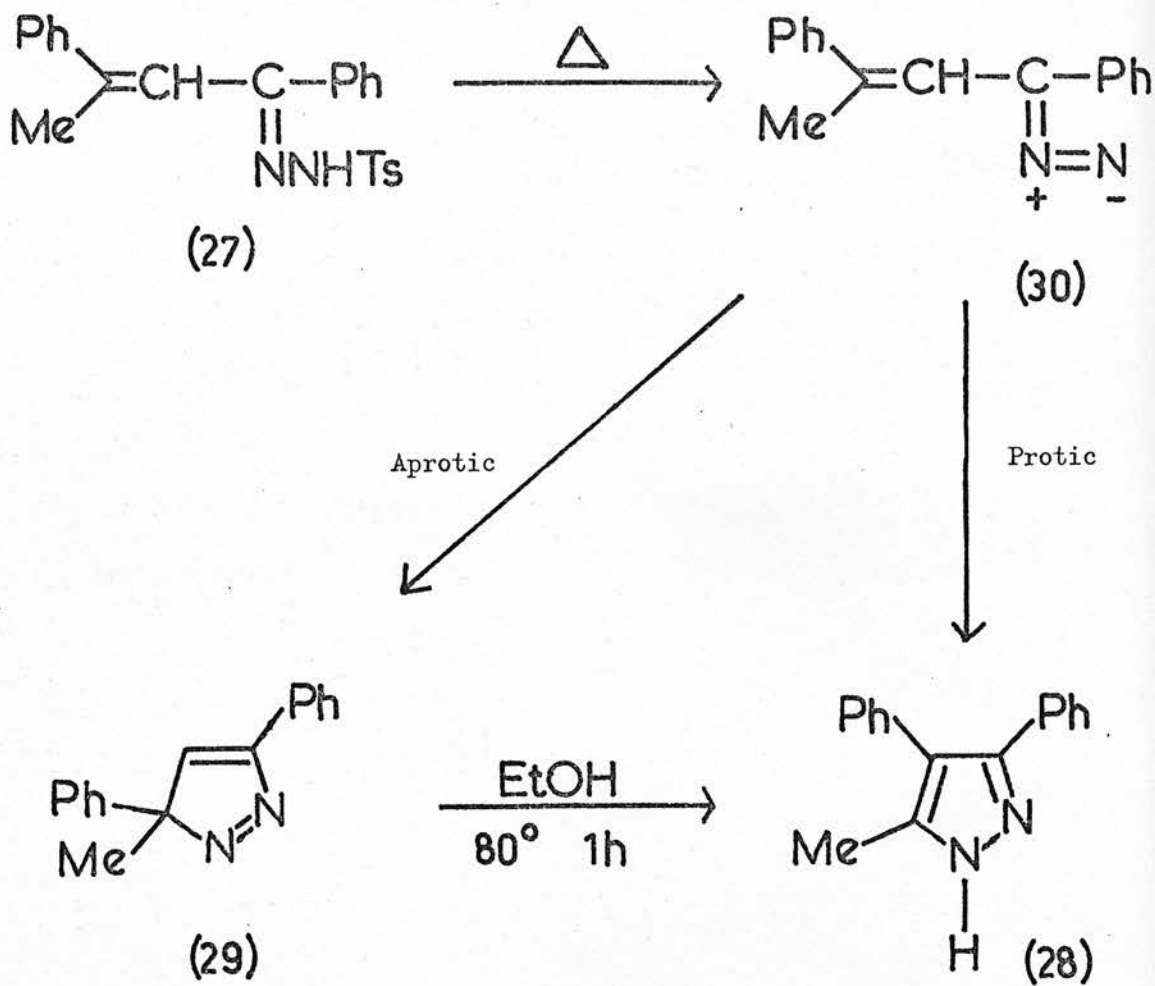
These workers thus showed that substitution of a methyl group for a hydrogen in position R¹ greatly increased the cyclopropene yield. Unfortunately, Closs and co-workers did not make much effort to determine the pyrazole yields.

The possibility that the 3H-pyrazole could give rise to the cyclopropene was rejected as 3,3,5-trimethylpyrazole (23) was stable under the reaction conditions.



Support for the carbene mechanism was found in that 4-methylpenta-1,3-diene (25) is formed in the decomposition of 4-methylpent-3-ene-2-one tosylhydrazone (26).





Scheme 7

The intermediacy of the diazoalkene was supported by reducing the tosylhydrazone decomposition temperature to 70-90°. Under these conditions, the diazoalkenes from compounds A and B (Table 1) were isolated. On pyrolysis, these diazoalkenes gave the cyclopropene as before.

To account for the large variation in cyclopropene yields, Closs and co-workers suggested that the behaviour of the diazoalkene is strongly dependent on the degree of substitution on the β -carbon of the tosylhydrazone. These workers maintain that both steric and electronic effects resulting from increasing methyl substitution at this position will retard the rate of cyclisation to the 3H-pyrazole. Elimination of nitrogen will be accelerated by the electron releasing power of the methyl groups.

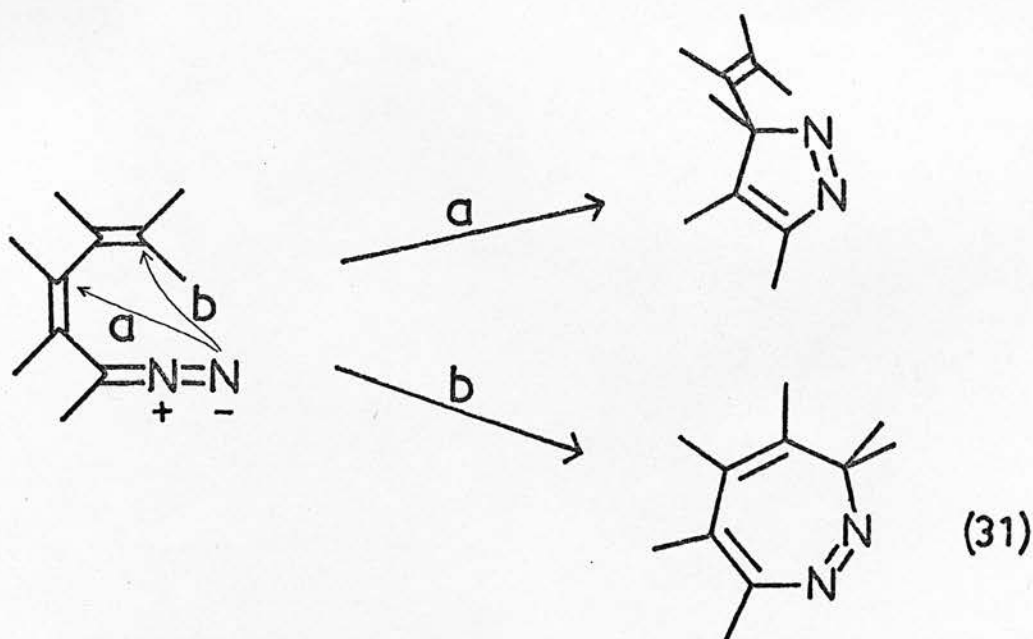
Sato and Watanabe³⁹ decomposed α -methylstyryl phenyl ketone tosylhydrazone (27) in both protic and aprotic solvents (Scheme 7). In protic solvent (sodium methoxide in ethylene glycol), the decomposition gave 5-methyl-3,4-diphenylpyrazole (28), while in aprotic conditions (sodium hydride in n-hexane) 3-methyl-3,5-diphenylpyrazole (29) was found. The 3H-pyrazole (29) could be rearranged to the 1H-pyrazole when it was heated in ethanol.

Thorogood⁴⁰ reinvestigated this system using the sodium salt of the tosylhydrazone as his starting material. He confirmed that the decomposition products in protic (ethanol) and aprotic (cyclohexane) solvents were as found by Sato and Watanabe³⁹ and showed that 1H-pyrazole (28) could be formed in aprotic solvent either from the tosylhydrazone salt or the 3H-pyrazole (29), provided the reaction was carried out at a high enough temperature (*i.e.* in boiling toluene, b.p. 111°). Such thermal and acid-catalysed rearrangements will be discussed in more detail in the next section.

No products derived from carbenes were found by either Sato and Watanabe³⁹ or Thorogood⁴⁰ in the decomposition of α -methylstyryl phenyl ketone tosylhydrazone. This is in contrast to the decompositions carried

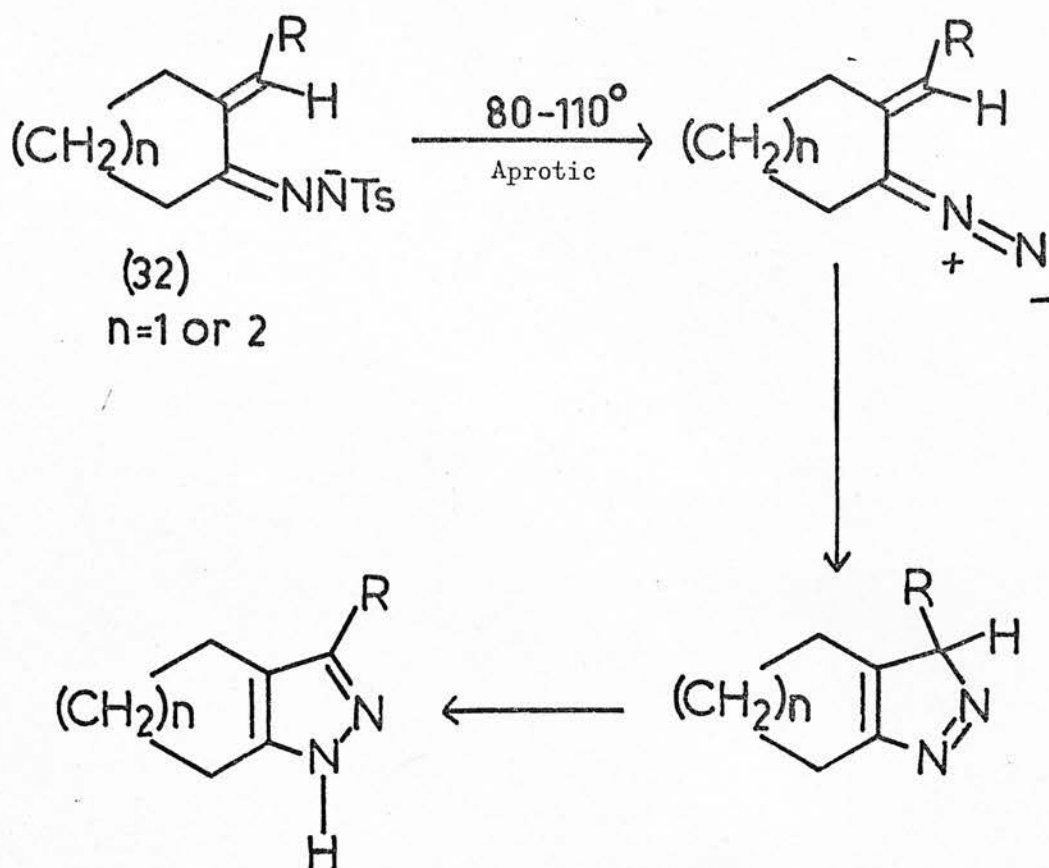
out by Closs and co-workers³⁸ who found that bulky groups on the β -carbon resulted in high yields of cyclopropenes. The difference in behaviour is probably due to the high temperatures (160–220°) used by Closs and co-workers, and also to the effects of the phenyl groups. The phenyl group on the diazo-carbon of the diazoalkene (30) will stabilise the intermediate,³⁷ while the phenyl on the β -carbon will increase the rate of cyclisation to the pyrazoles.¹³

These electrocyclic reactions can be extended to give seven membered ring products if molecules with suitable geometry are used. Sharp and co-

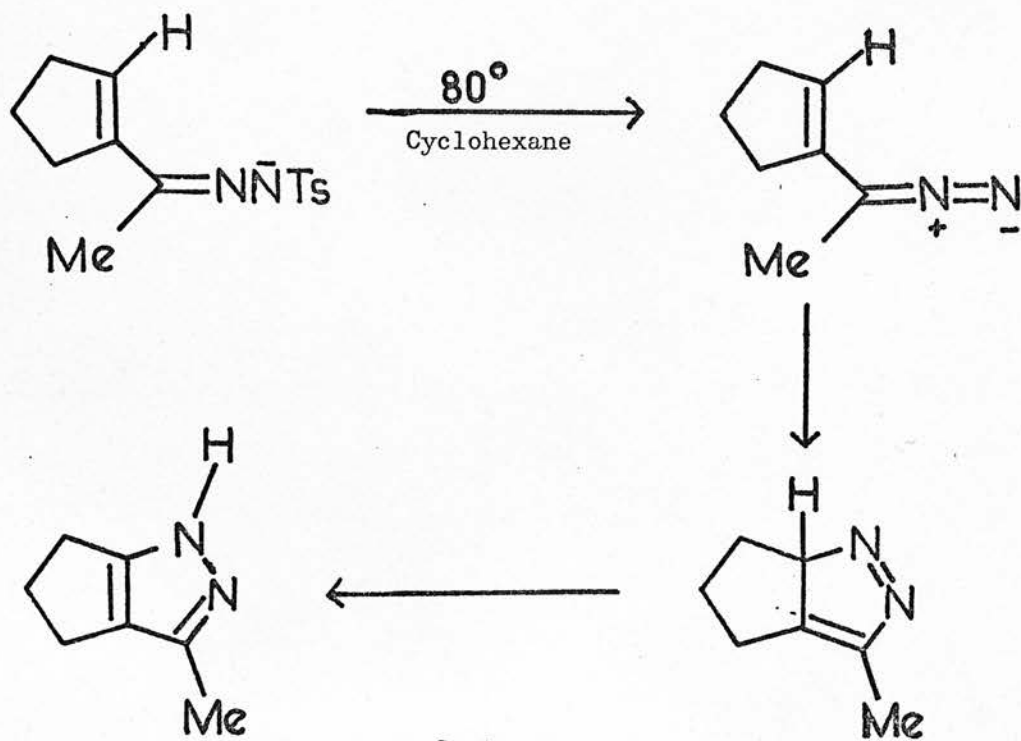


workers^{41,42} have cyclised aryl substituted diazoalkenes to give diazepines (31) when the geometry of the molecule was such that pyrazole formation was unfavourable. The decomposition of the $\alpha\beta$ -unsaturated tosylhydrazones of cyclic ketones⁴¹ has shown that the geometrical constraints on the resulting diazoalkene can be extremely important in determining its mode of decomposition.

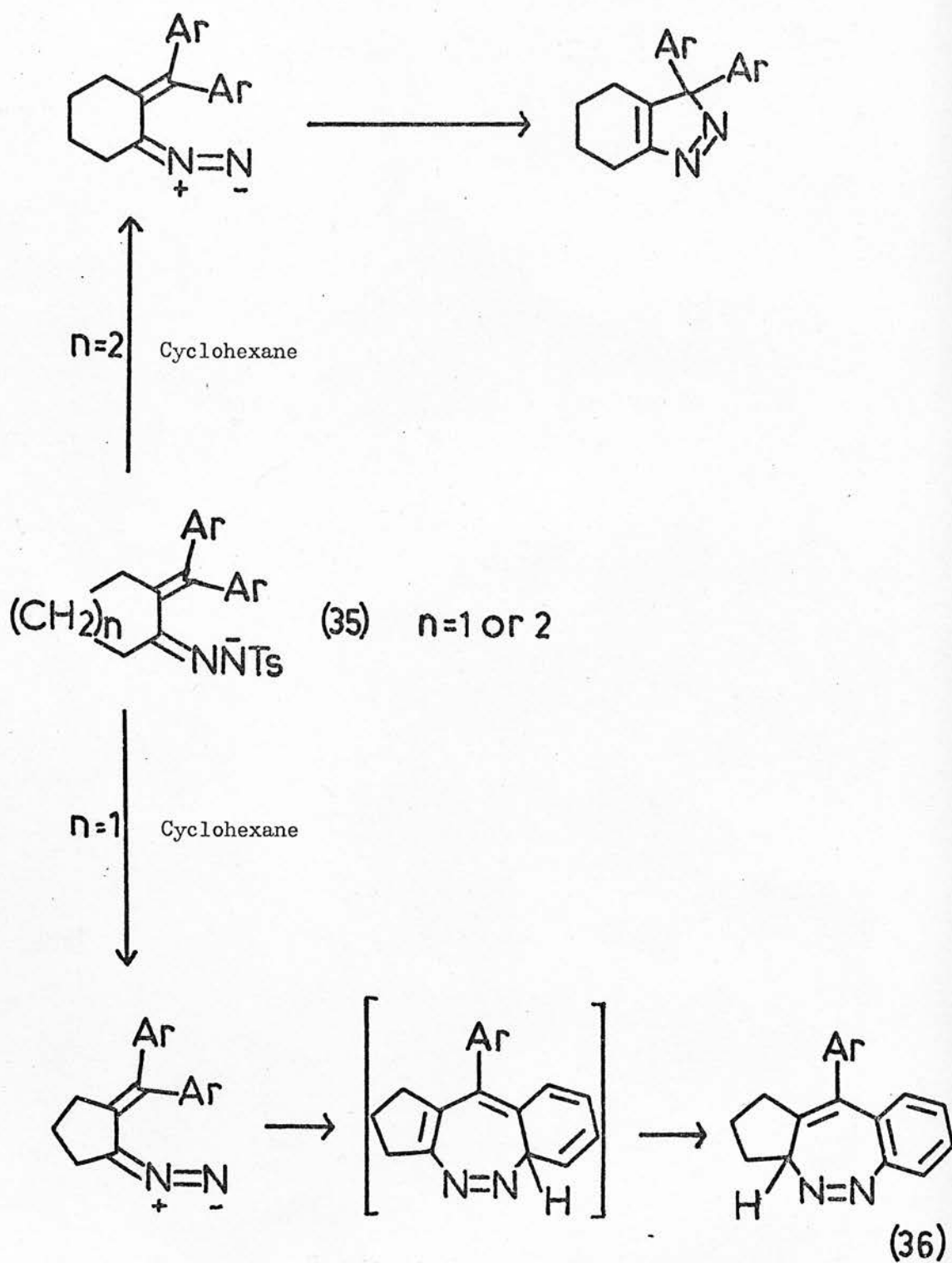
The decomposition of the tosylhydrazone salts which have a β -hydrogen atom (Scheme 8) are not, however, affected by the ring size. The sodium



Scheme 8



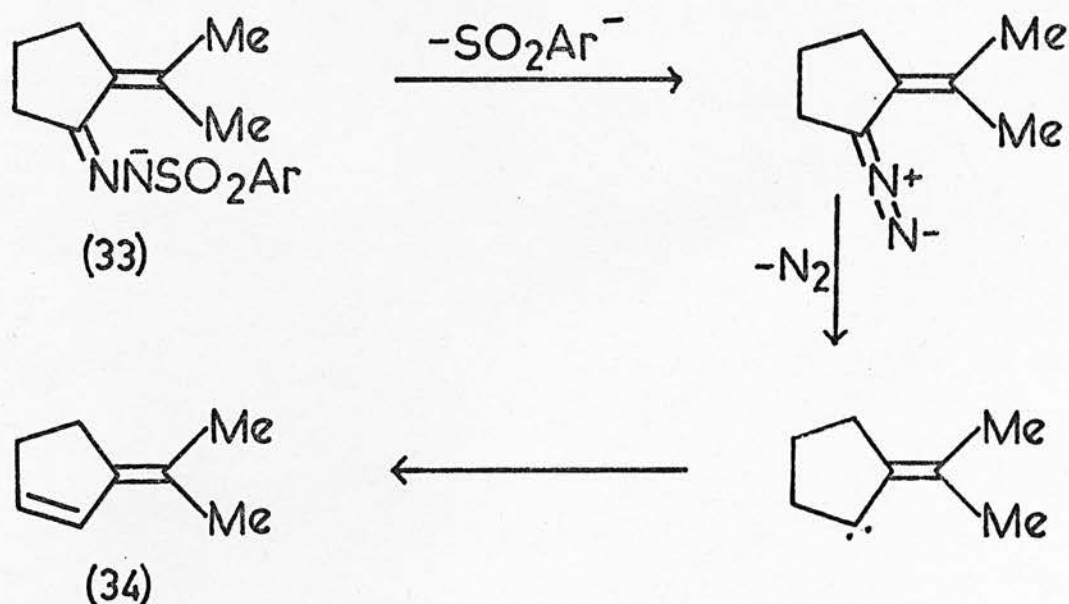
Scheme 9



Scheme 10

salts of 2-methylenecyclohexanone ($32, n=2$) and 2-methylenecyclopentanone ($32, n=1$) tosylhydrazones both decompose in aprotic solvents to give $1H$ -pyrazoles. Stanley⁴³ showed a similar result with 1-acetylcyclopentene tosylhydrazone (Scheme 9). In each of these cases the tosylhydrazone has a hydrogen atom on the β -carbon which can migrate to aromatise the $3H$ -pyrazole to the more stable $1H$ -pyrazole.

However, when there is no hydrogen on the β -carbon then the mode of reaction of the tosylhydrazone salt is strongly influenced by ring size. When 2-isopropylidenecyclopentanone tosylhydrazone (33) was decomposed, the diazoalkene lost nitrogen and the resultant carbene underwent a hydride shift to form the diene (34).

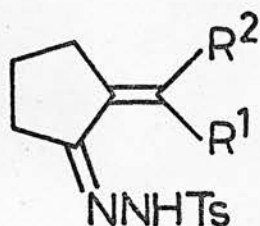


With two aryl groups on the methylene carbon of the tosylhydrazones (35, Scheme 10), Sharp and co-workers⁴¹ showed that a different mode of cyclisation became possible. With $n = 1$, the diazo group attacked the aromatic ring to form a diazepine (36).

A steric effect was postulated⁴¹ to account for the difference in behaviour between the cyclopentanones and the cyclohexanones. It was claimed that diazoalkenes having a six membered ring had a geometry which

facilitated cyclisation to the pyrazole, but that the five membered analogues were less well set up for such a reaction and decomposed by another route, i.e. to the diazepine (36) or the diene (34). This postulate about the molecular geometry will be amplified in the discussion section of this Thesis.

The only tosylhydrazones of types A & B which Thorogood⁴⁰ and Stanley⁴³ found which decomposed to give pyrazoles were those with $R^1 = H$, i.e. those which could undergo a hydrogen shift after cyclisation, to form aromatic 1H-pyrazoles.



A

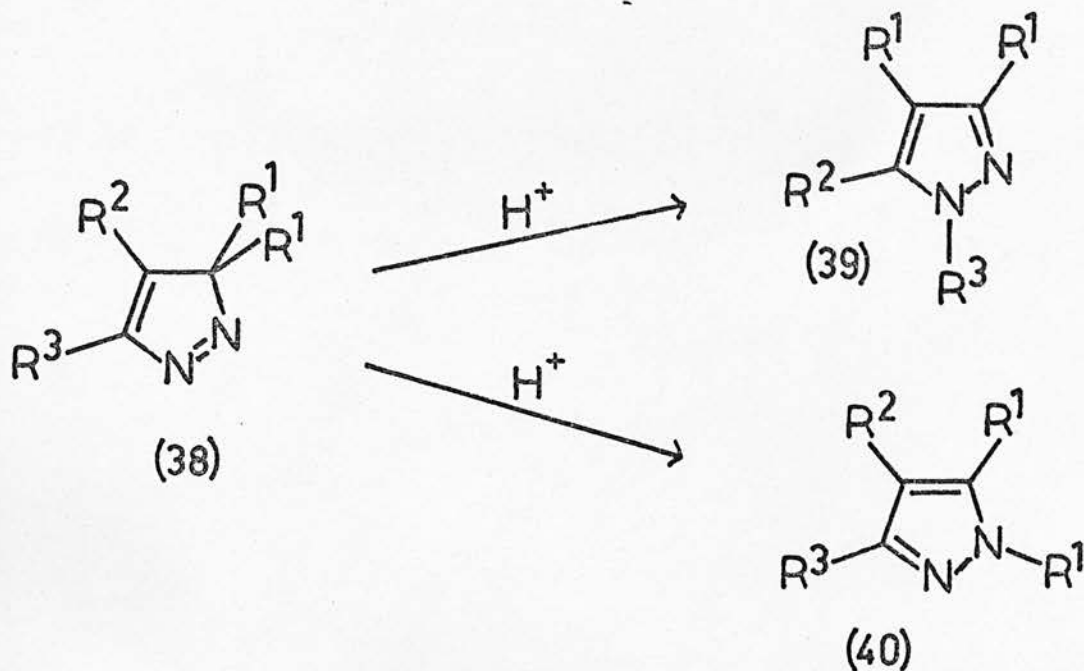


B

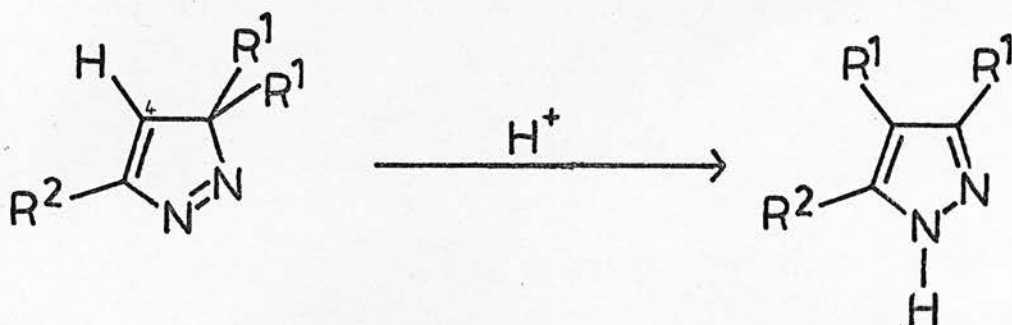
Cyclisations of diazoalkenes to give good yields of diazepines were also carried out by Stanley⁴³ with 2-diphenylmethyleindan-1-one tosylhydrazone (Scheme 11), and by Sharp and co-workers⁴⁴ with α -(p-alkenylaryl)-diazoalkanes (Scheme 12). The diazoalkene (37) does not cyclise to an indazole as such a mode of decomposition would result in an irrevocable loss of aromaticity.

REARRANGEMENT REACTIONS OF PYRAZOLES

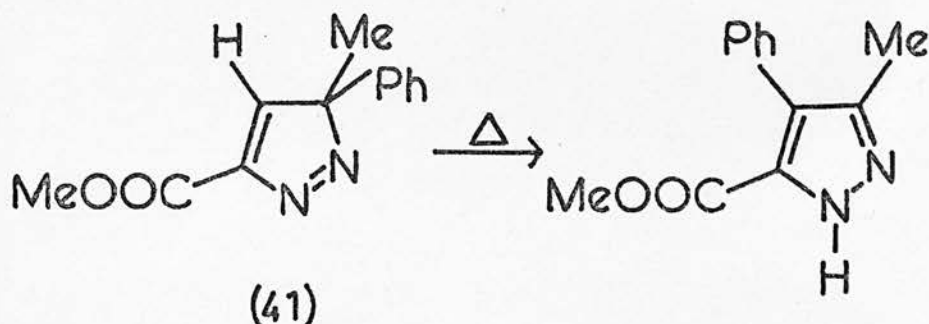
In 1943, van Alphen⁴⁵ studied the acid-catalysed rearrangements of 3H-pyrazoles and found that a large variety of 3H-pyrazoles gave 1H-pyrazoles when heated in acetic acid. He reported that 3,3,4,5-tetrasubstituted 3H-pyrazoles (38) could give either of the 1H-pyrazoles (39) and (40).



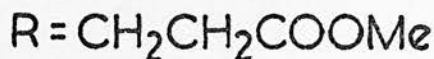
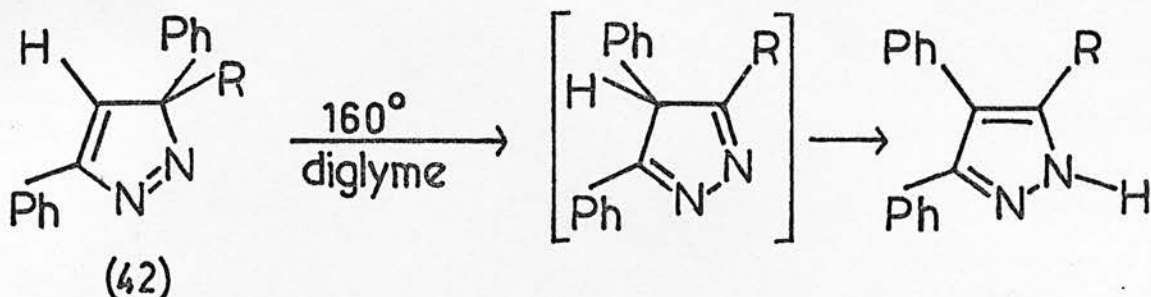
With 3,3,5-trisubstituted 3H-pyrazoles, van Alphen showed that migration of R¹ was followed by migration of the hydrogen on C4 to give the 1H-pyrazole.



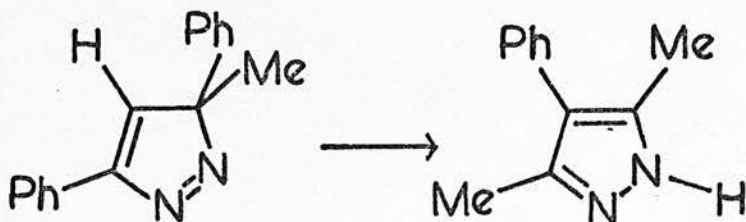
In 1960, Hüttel and co-workers⁴⁶ continued the study of acid-catalysed rearrangements, the results of which were in general agreement with those of van Alphen.⁴⁵ They also carried out some thermal rearrangements of 3H-pyrazoles (41) in the absence of acid, and concluded that a phenyl group migrates more readily than a methyl, both in the acid-catalysed and the thermal rearrangements.



Moritani⁴⁷ heated the 3H-pyrazole (42) and postulated an unstable 4H-pyrazole intermediate in the rearrangement to the stable 1H-pyrazole.



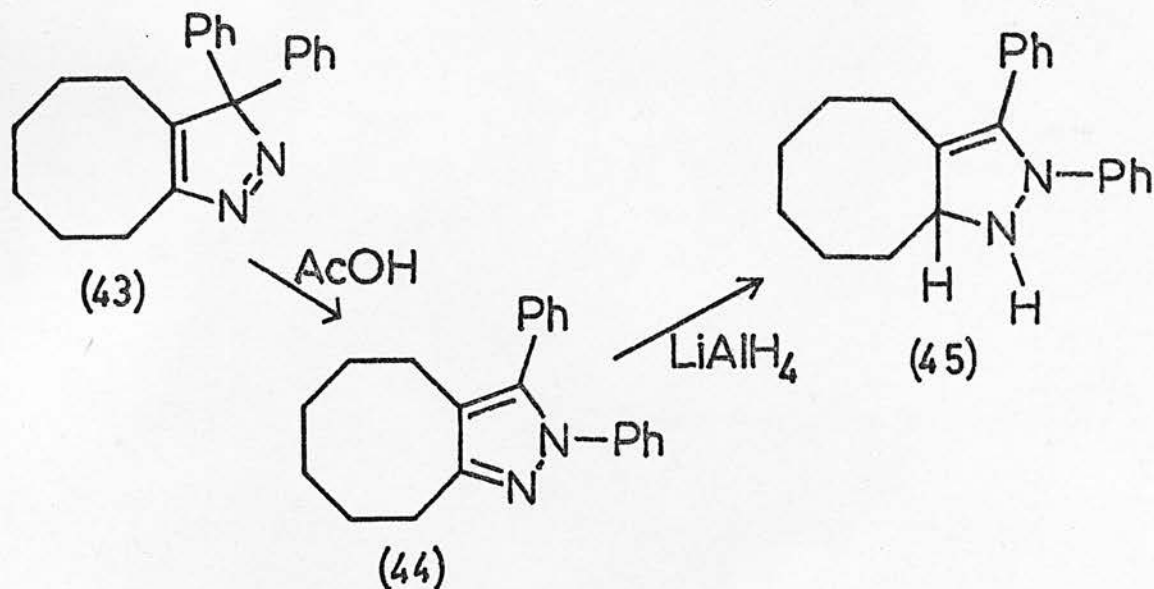
A similar acid-catalysed rearrangement was carried out by Sato and Watanabe³⁹ on heating 3-methyl-3,5-diphenylpyrazole in boiling ethanol (the ethanol being sufficiently acidic to catalyse the reaction), and Thorogood⁴⁰ effected the same reaction thermally, in boiling toluene. This further illustrates the preferential migration of a phenyl over a methyl group, as



found by Hüttel.⁴⁶

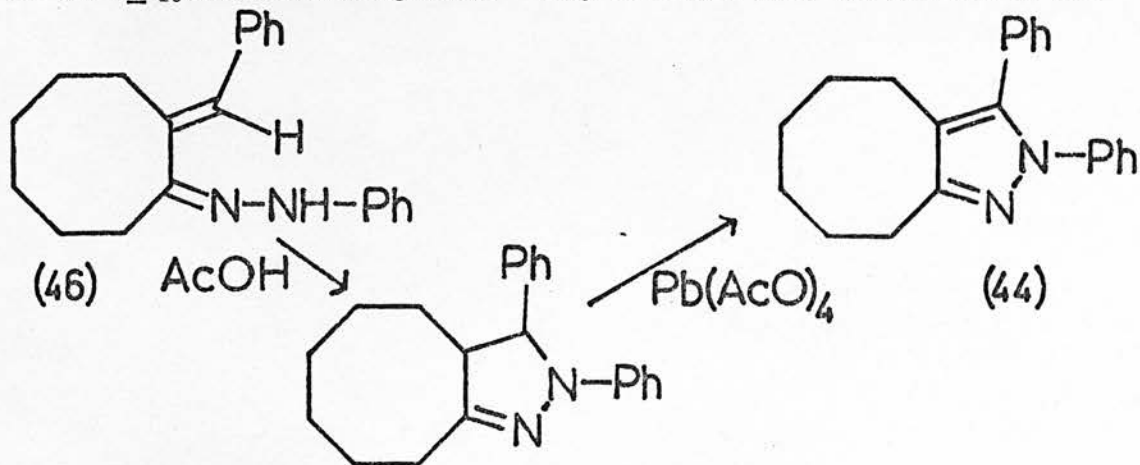
The preparation of 1H-pyrazoles from 3H-pyrazoles has been reviewed by Fusco.⁴⁸

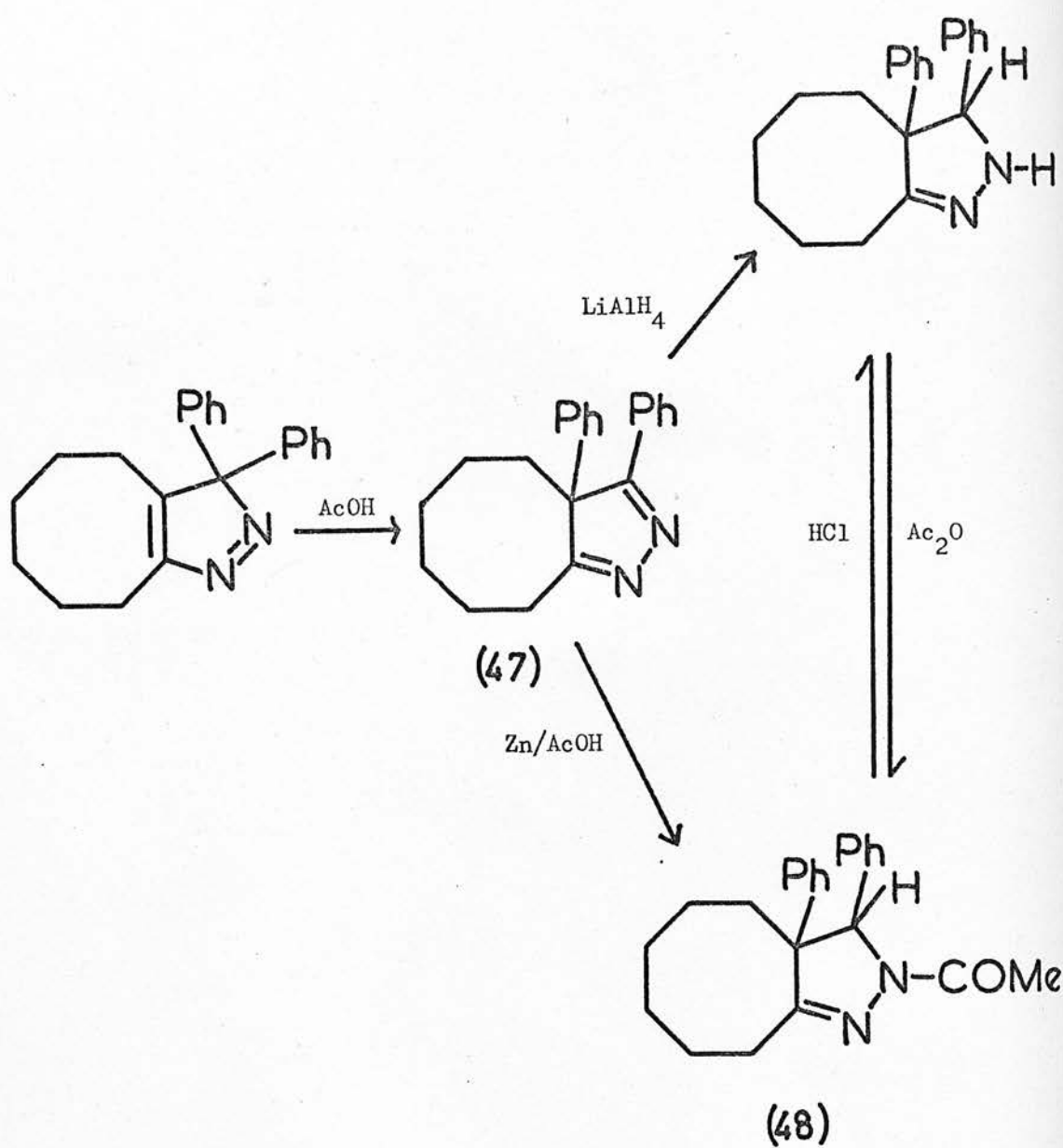
Wittig and Hutchison⁴⁹ rearranged the 3H-pyrazole (43) by heating in acetic acid. They claimed that the product was the 1H-pyrazole (44) as would be predicted from the work of van Alphen.⁴⁵ To further characterise their product (44), these workers formed pyrazoline (45) by reduction. Jacquier



and co-workers⁵⁰ have recently repeated these reactions, using the same conditions as Wittig and Hutchison.⁴⁹ They produced identical products but dispute the structures (44) and (45) assigned by the earlier workers.

Jacquier's group synthesised an authentic sample of the pyrazole (44) from the phenylhydrazone (46), and found that it was not identical with the product of the 3H-pyrazole rearrangement. They concluded that the product of the

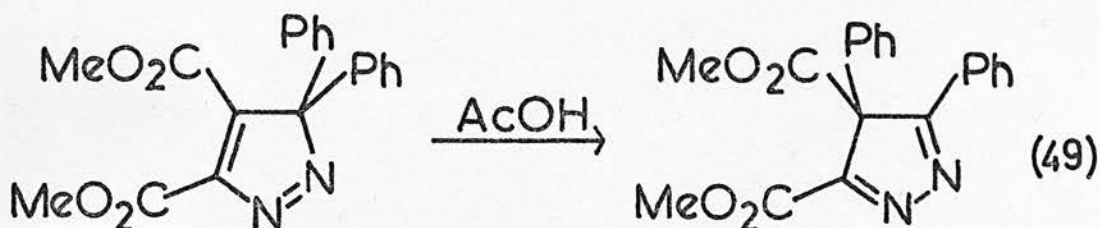




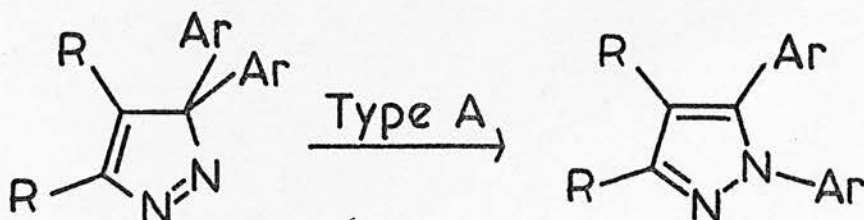
Scheme 13

pyrazole (43) rearrangement was therefore not (44) but the 4H-pyrazole (47, Scheme 13), which they characterised by reduction to the pyrazoline (48) in zinc and acetic acid.

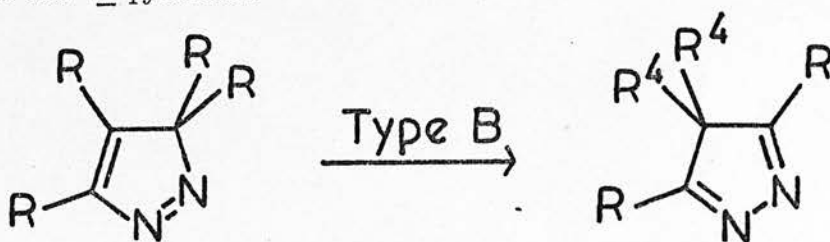
Jacquier and co-workers⁵¹ have more recently shown that a 3H-pyrazole can rearrange to a 4H-pyrazole (49) even when it contains an ester group. According to van Alphen and Hüttel, such an ester group would readily migrate

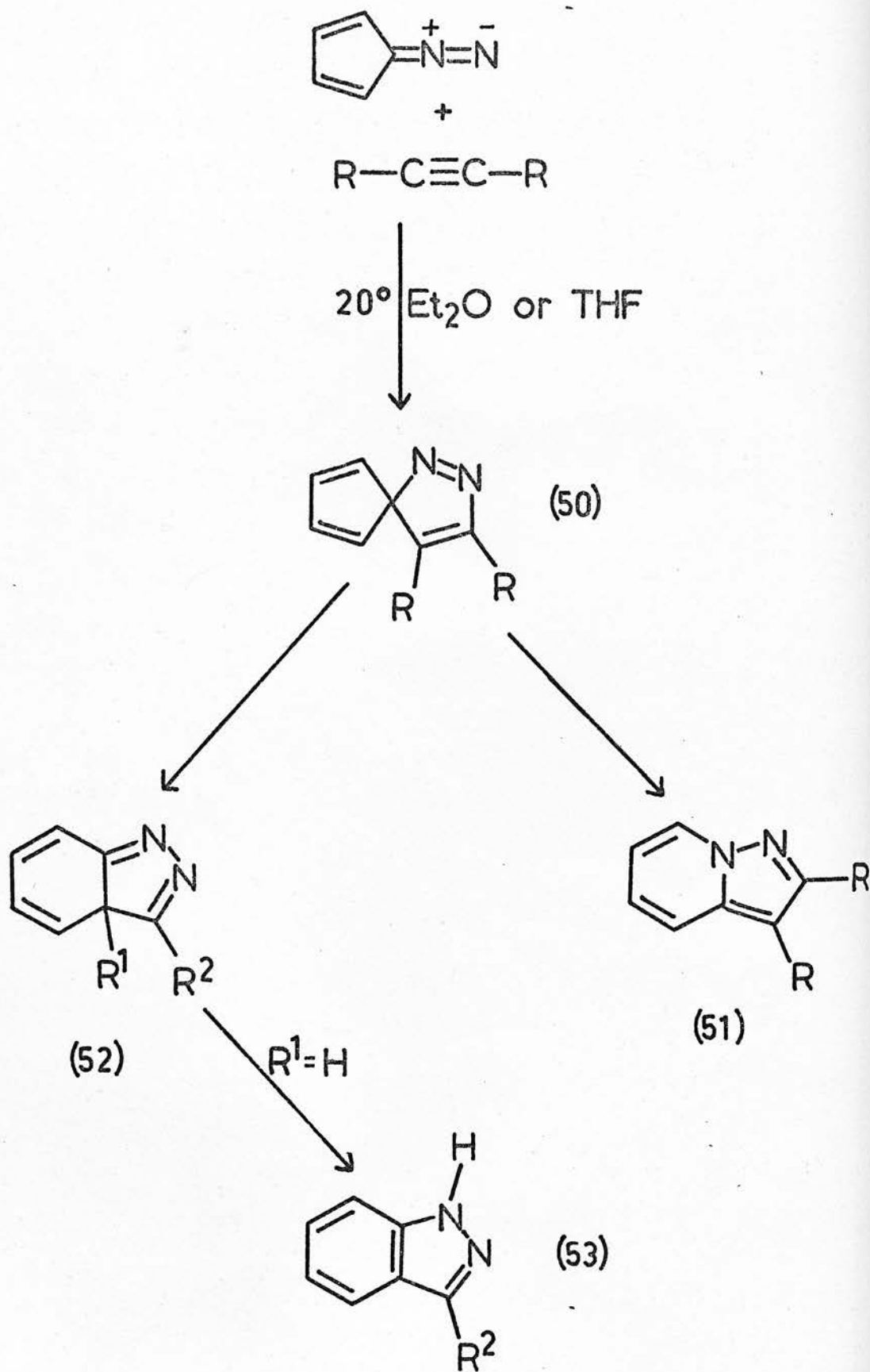


to give a 1H-pyrazole. From both the thermal and the acid-catalysed rearrangements of 3H-pyrazoles, Jacquier has concluded that if both the substituents on C-3 are aryl, it may be possible for a rearrangement of type A to occur, but in other cases, the rearrangement (type B) goes to the



4H-pyrazole, which will be stable if R^4 is alkyl or aryl. If $R^4 = H$, the 4H-pyrazole is isomerised to the 1H-pyrazole, and if R^4 is an ester group, the pyrazole will rearrange under drastic conditions of heating or acidity to give the 1H-pyrazole.

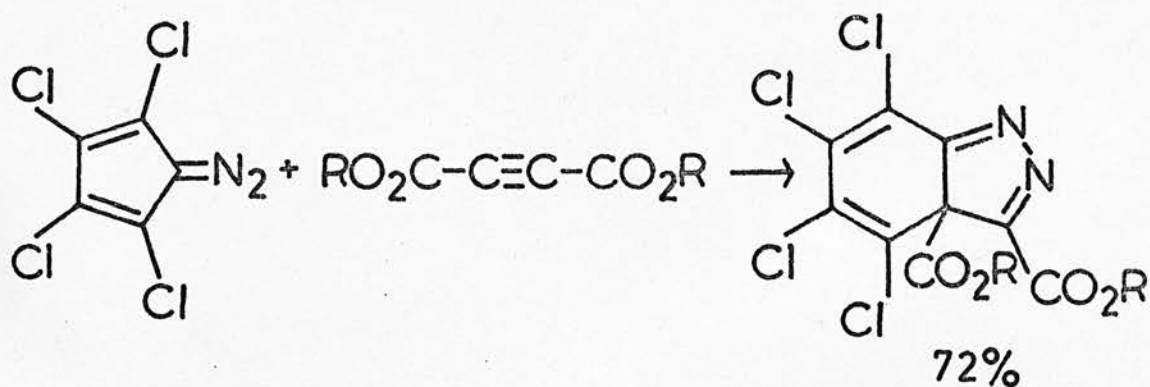




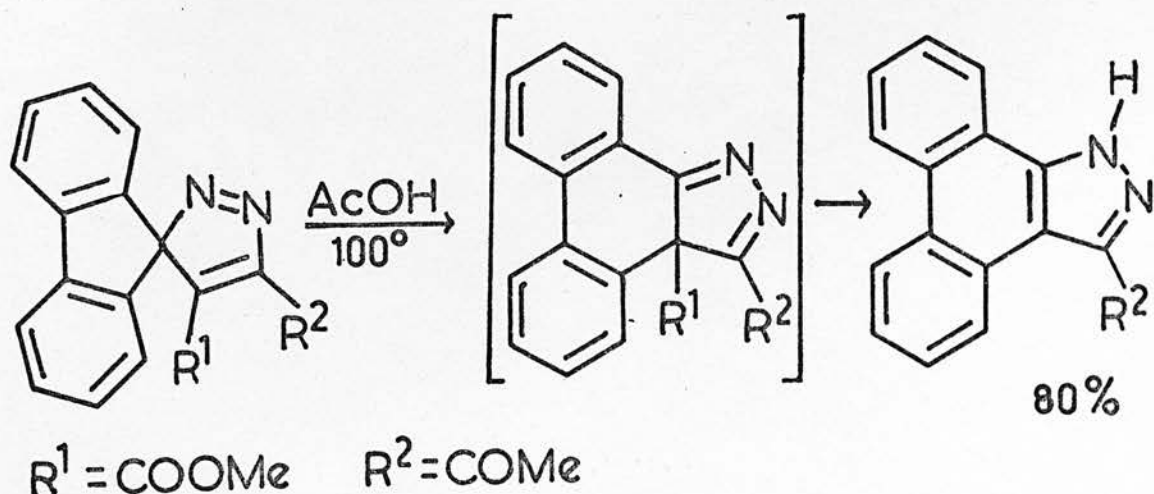
Scheme 14

In the light of Jacquier's works, it would be of interest to reinvestigate earlier rearrangements in order to ascertain that the correct structures have been assigned to the products. It would appear, however, that the main reason why van Alphen⁴⁵ and Hüttel⁴⁶ did not isolate compounds to which they assigned the structures of 4H-pyrazoles, was that they happened to study compounds which rearrange to 1H-pyrazoles.

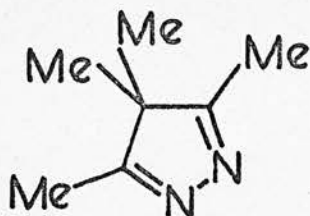
Dürr and co-workers^{52,53,54} have recently carried out a series of rearrangements of spiro-3H-pyrazoles. 1,3-Dipolar cycloaddition of diazo-cyclopentadienes to alkynes at room temperature led to the isolation of spiro-3H-pyrazoles (50), azaindolizines (51), 3aH-indazoles (52) and 1H-indazoles (53, Scheme 14). Under these mild conditions, Dürr was able to isolate a 3aH-indazole with R¹ = ester. Under more vigorous conditions,



such an ester group decarboxylates, and the compound rearranges to the 1H-indazole.⁵⁴



Grigg and co-workers⁵⁵ have shown that 3,4,4,5-tetramethylpyrazole (54) is little changed on heating at 280°.



(54)

Thus, in recent years it has become apparent that 4H-pyrazoles with no hydrogen on C4 are more stable, relative to 1H-pyrazoles than had previously been thought. The rearrangement reactions of 3H-pyrazoles may well all go via or to the 4H-pyrazoles, and the early work which claims to involve the migration of an aryl group on C3 to nitrogen^{45,46} needs to be reinvestigated to determine if the assigned structures are correct.

EXPERIMENTAL

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PREPARATION AND DECOMPOSITION OF THE SODIUM SALTS OF THE
TOSYLHYDRAZONES, AND RELATED REACTIONS

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General Method of Preparation and Decomposition of the
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SYMBOLS AND ABBREVIATIONS

The symbols used in this Thesis are those in common usage. In addition, the following symbols are used:

| | |
|-------------|--|
| R_f | ratio of distance moved by the substance to distance moved by the solvent front. |
| h.s.l.c. | high-speed liquid chromatography. |
| g.l.c.-m.s. | gas liquid chromatography coupled to high resolution mass spectrometry. |
| DME | 1,2-dimethoxyethane. |
| d | decomposition. |
| bs | broad singlet. |

INSTRUMENTATION AND TECHNIQUES

Gas Liquid Chromatography.

Analytical investigations were carried out on either a Pye Series 104 chromatograph, using 4 mm internal diameter packed columns of length 1.5 m, or a Perkin-Elmer F.11 chromatograph, using 2.2 mm x 2 m packed columns. Both chromatographs used a flame ionisation detector and nitrogen carrier gas. The following stationary phases, supported on 100-200 mesh celite were employed: neopentylglycol succinate (NPGS), silicone elastomer (SE 30), carbowax, silicone oil (OV 1) and Apiezon grease (APL).

High-Speed Liquid Chromatography.

A Cecil Instruments CE 212 ultraviolet detector was used, operating with a constant pressure pump by Applied Research Laboratories. A steel column, 3 mm x 50 cm, and a glass column, 5 mm x 15 cm were used, both packed with Phasesep Spherisorb alumina of particle diameter 20 μ m.

Column Chromatography.

Alumina was Spence and Sons, Grade H, 100-200 mesh (Brockmann activity = I). For dry column chromatography,⁵⁶ this alumina was treated with 6% water to reduce the Brockmann activity to III. Nylon tubing was supplied by Walter Coles and Co. Ltd., London.

Thin Layer Chromatography.

Chromatograms were obtained on 0.33 mm or 1.0 mm (preparative) layers of alumina (Merck, Aluminium oxide G) or silica gel (Merck, Kieselgel G). Components in the developed chromatogram were detected by their fluorescence in ultraviolet light, or by their reaction with iodine.

Nuclear Magnetic Resonance Spectroscopy.

Proton magnetic resonance spectra were run on a Perkin-Elmer model R 10, operated by Mr. T.W. Naisby, or a Varian EM 360 spectrometer, operating at a frequency of 60 MHz. In addition, a Varian HA 100 spectrometer, operated by Mrs. M.N. Groves and Mr. J.R.A. Miller, was used for decoupling experiments and when high resolution was required. ^{13}C Magnetic resonance spectra were obtained using a Varian XL 100 spectrometer, operated by Mr. A.S.F. Boyd. Chemical shifts in proton spectra were recorded as tau (τ) values, and in ^{13}C spectra, as parts per million (p.p.m.), tetramethylsilane being the internal reference.

Mass Spectrometry.

Mass spectra were obtained using an Associated Electrical Industries MS 902 spectrometer, operated by Mr. D.J.A. Thomas, or using an Associated Electrical Industries MS 20 spectrometer coupled to a Pye Series 104 gas chromatograph. In the latter case, the carrier gas was helium and the flow rate was 40 ml/min.

Infrared Spectroscopy.

Liquid samples were examined as thin films and solid samples as nujol mulls, both on polished sodium chloride plates, using Perkin-Elmer 337 and 157G grating spectrometers.

Ultraviolet Spectroscopy.

A matched pair of 1 cm silica cells were used in either a Perkin-Elmer 137 or a Unicam SP 800 spectrophotometer.

Melting Points.

The melting points of all new compounds were obtained with the sample

in a capillary tube.

Elemental Analysis.

Microanalyses were carried out by Mr. J. Grunbaum using a Perkin-Elmer model 240 analyser, or by the National Physical Laboratory.

Drying.

Anhydrous magnesium sulphate was used to dry all organic solutions, unless otherwise stated.

Distillation.

Mixtures of isomeric ketones with similar boiling points were separated by use of a Fischer Spaltrohr System MMS 200 distillation apparatus.

Purification of Reagents and Solvents.

"Super-dry" ethanol was prepared as described by Vogel⁵⁷ (method 1).

1,2-Dimethoxyethane and cyclohexane were dried over sodium wire and then stored over calcium hydride under nitrogen. The solvents were freshly distilled from the calcium hydride as required.

Tri-n-butylphosphine was dried over magnesium sulphate, and then distilled under dry nitrogen, and the fraction b.p. $130^{\circ}/20$ mm retained and stored under dry nitrogen at -20° .

Petroleum refers to the fraction b.p. $40-60^{\circ}$ unless otherwise stated.

PREPARATION OF STARTING MATERIALS

1. Adipyl chloride.⁵⁸ Adipic acid (112.7 g, 0.77 mol) was added to a flask containing thionyl chloride (270 ml, 4 mol) in benzene (300 ml). The mixture was heated under reflux for 12 h, then the benzene was evaporated under reduced pressure and the residue was distilled to give adipyl chloride (144 g, 100%), b.p. 120–124°/15 mm Hg.
2. 1,4-Dibenzoylbutane (39%), m.p. 104–107° (lit.,⁵⁸ 104–107°) was prepared by the Friedel-Crafts acylation of benzene with adipyl chloride,⁵⁸ i.r. 1675 cm⁻¹ (C = O).
3. 1-Phenylcyclopentene (56%), b.p. 52–64°/0.2 mm Hg (lit.,⁵⁹ 72–74°/1.5 mm Hg) was prepared by the reaction of phenyl magnesium bromide with cyclopentanone.⁵⁹ ¹H N.m.r. (CCl₄): τ 2.4–3.0 (m, 5H), 3.9 (m, 1H), 7.2–7.6 (m, 4H), 7.9–8.2 (m, 2H).
4. 1-p-Tolylcyclopentene (40%), b.p. 66–74°/0.4 mm Hg (lit.,⁵⁹ 96–100°/2.5 mm Hg) was prepared in collaboration with Mr. T.W. Naisby by the reaction of p-tolyl magnesium bromide with cyclopentanone.⁵⁹ ¹H N.m.r. (CCl₄): τ 2.82 (d, J 8 Hz, 2H), 3.06 (d, J 8 Hz, 2H), 4.02 (m, 1H), 7.3–7.6 (m, 4H), 7.73 (s, CH₃), 7.8–8.2 (m, 2H).
5. 1-p-Fluorophenylcyclopentene (49%), b.p. 128–136°/16 mm Hg (lit.,⁶⁰ 230°/760 mm Hg) was prepared in collaboration with Mr. T.W. Naisby by the reaction of p-fluorophenyl magnesium bromide with cyclopentanone.⁵⁹
6. 1-Phenylcyclohexene (74%), b.p. 69–72°/0.3 mm Hg (lit.,⁵⁹ 71°/0.6 mm Hg) was prepared by the reaction of phenyl magnesium bromide with cyclo-

hexanone.⁵⁹

7. 3-Phenylindene (56%), b.p. 122-126°/0.7 mm Hg (lit.,⁶¹ 200-201°/29 mm Hg) was prepared in collaboration with Mr. T.W. Naisby by the reaction of phenyl magnesium bromide with indan-1-one.⁵⁹

8. 4-Carbethoxy-3-methylcyclohex-2-enone (40%), b.p. 124-150°/11 mm Hg (lit.,⁶² 142-144°/15 mm Hg) was prepared by the condensation of para-formaldehyde with two moles of acetoacetic ester.⁶² I.r. 1730 (C = O, ester), 1675 (C = O), 1630 cm⁻¹ (C = C). ¹H.N.m.r. (CDCl₃): τ 4.06 (s, 1H), 5.81 (q, J 7Hz, 2H), 6.74 (m, 1H), 7.3-8.0 (m, 4H), 7.98 (s, CH₃), 8.73 (t, J 7Hz, 3H).

9. Phenylbromoethyne (53%), b.p. 40-50°/3.5 mm Hg (lit.,⁶³ 40-41°/0.1 mm Hg) was prepared by Mr. K.A. Wall,⁶⁴ by the reaction of bromine with freshly distilled phenylacetylene.⁶³

10. Triphenyl(phenylethynyl)phosphonium bromide (100%), m.p. 118-125° was prepared by Mr. K.A. Wall.⁶⁴ Triphenylphosphine was reacted with phenylbromoethyne⁶⁵ in tetrahydrofuran which had been purified by passing down an activated alumina column.

11. 2-Ethoxycarbonylcyclohexanone (44%), b.p. 72°/0.4 mm Hg (lit.,⁴⁰ 94-96°/7 mm Hg) was prepared in collaboration with Mr. T.W. Naisby by the reaction of diethyl oxalate and cyclohexanone in the presence of base.⁴⁰ The product was distilled on a Nester-Faust spinning-band apparatus.

12. 2-Ethylenedioxyethoxycarbonylcyclohexane (61%), b.p. 131-132°/9 mm Hg

(lit.,⁴⁰ 126-127°/8 mm Hg) was prepared in collaboration with Mr. T.W. Naisby by the condensation of 2-ethoxycarbonylcyclohexanone and ethylene glycol.⁴⁰

13. 1-Morpholinocyclohexene (85%), b.p. 119-121°/11 mm Hg (lit.,⁶⁶ 118-120°/10 mm Hg) was prepared in collaboration with Mr. T.W. Naisby by the condensation of morpholine and cyclohexanone.⁶⁶

14. 2-Acetylcyclohexanone (37%), b.p. 96-98°/10 mm Hg (lit.,⁶⁷ 103-106°/10 mm Hg) was prepared in collaboration with Mr. T.W. Naisby by the acetylation of 1-morpholinocyclohexene.⁶⁷

15. Mixture of 4,5,6,7-Tetrahydro-3-methyl-1-phenylindazole and 4,5,6,7-Tetrahydro-3-methyl-2-phenylindazole. This mixture was prepared by an adaptation of the methods of Eistert and Wessendorf,⁶⁷ and Jacquier and Maury.⁶⁸ Phenylhydrazine (0.5 g, 4.6 mmol) was dissolved in ethanol (7 ml) and concentrated sulphuric acid (1 ml) was added to the solution. 2-Acetylcyclohexanone (0.6 g, 4.3 m moles) was then added and the solution was heated until it boiled and then cooled immediately. Examination of the solution by t.l.c. (silica/benzene) showed no residual diketone. The solution was then neutralised with dilute sodium hydroxide solution, and the organic material was extracted with ether. The solvent was removed to leave a brown oil (872 mg, 100%). A sample was purified by dry column chromatography (alumina/methylene chloride) (Found: C, 79.4; H, 7.8; N, 13.0. $C_{14}H_{16}N_2$ requires C, 79.2; H, 7.6; N, 13.2%). ¹H N.m.r. and ¹³C n.m.r. spectra: see Appendix. Mass spectrum: m/e 212 (100), 184 (38). (Found: 212.130671, 184.099656. $C_{14}H_{16}N_2$ requires 212.131342. $C_{12}H_{12}N_2$ requires 184.100043.

PREPARATION OF $\alpha\beta$ -UNSATURATED CARBONYL
COMPOUNDS, AND THEIR TOSYLHYDRAZONES

General Method of Preparation of the Tosylhydrazones.

Unless otherwise stated, the tosylhydrazones were prepared by the following method.

A solution of tosylhydrazide dissolved in the minimum quantity of ethanol was added to an equimolar quantity of the ketone (or a solution of the ketone in the minimum quantity of ethanol in the case of solid ketones) at 50°. The solution was allowed to stand at room temperature until the condensation was complete. On occasions, concentrated hydrochloric acid (1 or 2 drops) was added as a catalyst. If the mixture was left for more than an hour (some were left for three weeks), the reaction was left in the dark. The precipitated tosylhydrazone was then filtered off, washed with dry ether, dried and weighed. The tosylhydrazone was reacted in this state unless otherwise stated, and a small sample was recrystallised for elemental analysis and melting point determination.

1. 1-Benzoyl-2-phenylcyclopentene.⁶⁹ 1,4-Dibenzoylbutane (51.7 g, 0.19 mol) and potassium hydroxide (36.2 g, 0.65 mol) were heated under reflux in ethanol (250 ml) for 48 h. The ethanol was then evaporated under reduced pressure and the residue was neutralised with dilute sulphuric acid. The product was extracted with ether, washed with water, dried, filtered and the solvent evaporated under reduced pressure. The residue was distilled to give a clear red oil (33.0 g) b.p. 144–156°/11 mm Hg which contained a mixture of 1-benzoyl-2-phenylcyclopentene and 3-benzoyl-2-phenylcyclopentene. Some of the latter was removed from the mixture by crystallisation from a mixture of petroleum and ether.

The mixture was then separated by dry column chromatography (alumina/benzene) to give 1-benzoyl-2-phenylcyclopentene as a waxy solid (5.9 g, 13%). $^1\text{Hn.m.r.}$ (CCl_4): τ 2.2-3.1 (m, 10H), 6.9-7.2 (m, 5H), 7.93 (quintet, J 8Hz, 2H). I.r. (nujol): 1650 (C = O), 1601, 1582, 1495, 1448, 1176, 1072, 692 cm^{-1} , identical with reported spectrum.⁶⁹

The tosylhydrazone (56%) was recrystallised from a mixture of ethanol (2 parts) and benzene (1 part) to give white crystals m.p. 145-148(d). (Found: C, 72.0; H, 5.9; N, 6.7. $\text{C}_{25}\text{H}_{24}\text{N}_2\text{SO}_2$ requires C, 72.1; H, 5.8; N, 6.7%). I.r. and $^1\text{Hn.m.r.}$ spectra: see Appendix.

2. 1-Acetyl-2-methylcyclopentene.^{70,71} Sodium (46 g, 2 mol) was dissolved in ethanol (650 ml) and the resulting solution was cooled to room temperature. Ethyl acetoacetate (260 g, 2 mol) was slowly added, followed by 1,2-dibromoethane (190 g, 1 mol); in both cases the rate being such that the temperature did not rise above 35°. The solution was then heated under reflux for 5 h, after which the ethanol was evaporated under reduced pressure. Sufficient water was added to dissolve the sodium bromide and the product was extracted with ether. The ether was then evaporated under reduced pressure to leave a brown oil (240 g). The major impurities in this oil were removed by steam distillation and discarded. The residue was extracted with ether, washed with dilute sodium carbonate solution, dried over anhydrous potassium carbonate, filtered and the ether evaporated under reduced pressure to leave crude ethyl diacetyl adipate (61 g) as a brown oil. 10% Sulphuric acid (450 ml) was added to this oil and the mixture was heated under reflux for 48 h. 1-Acetyl-2-methylcyclopentene was steam distilled. The distillate was saturated with ammonium sulphate, and the ketone extracted with ether, dried and the solvent evaporated under reduced pressure. The residue was distilled to give 1-acetyl-2-methylcyclopentene

(13.23 g, 11%), b.p. 69-74°/11 mm Hg [lit.,⁷¹ 189°/760 mm Hg]. I.r.⁷² 1679 (C = O, *s-cis*), 1657 (C = O, *s-trans*), 1615 cm⁻¹ (C = C). ¹Hn.m.r. (CCl₄): τ 7.2-7.7 (m, 4H), 7.88 (s, CH₃), 7.97 (s, CH₃), 8.0-8.3 (m, 2H).

The tosylhydrazone (60%) was recrystallised from ethanol to give white crystals m.p. 122-123 (d). (Found: C, 61.8; H, 6.6; N, 9.7. C₁₅H₂₀N₂SO₂ requires C, 61.6; H, 6.9; N, 9.6%). I.r. and ¹Hn.m.r. spectra: see Appendix.

3. 1-Acetyl-2-phenylcyclopentene was prepared by an adaptation of the method of Groves and Jones.⁷³ Acetic anhydride (60.3 g, 0.592 mol) and 1-phenylcyclopentene (80 g, 0.555 mol) were dissolved in carbon disulphide (250 ml). While the solution was stirred at 0°, zinc chloride (80.7 g, 0.592 mol) was slowly added. The reaction was monitored by g.l.c. (2½% OV 1/166°). After 24 h, when no more ketone was being formed, the mixture was poured into a mixture of ice and water. The product was extracted with ether, washed with water, dilute potassium bicarbonate solution, water again, and was then dried and filtered. The solvent was removed under reduced pressure to leave a red-brown oil (106.2 g), which was distilled to give 3-acetyl-2-phenylcyclopentene⁷⁴ (31.8 g, 31%) b.p. 83-102°/0.06 mm Hg. This was shown to be pure by g.l.c. (2% NPGS/170°). I.r. 1710 cm⁻¹ (C = O). ¹Hn.m.r. (CDCl₃): τ 2.6-2.9 (m, 5H), 3.7 (m, 1H), 6.2 (m, 1H), 7.3-8.0 (m, 4H), 8.1 (s, CH₃). G.l.c.-m.s. (2½% OV 1/166°), M⁺ 186.

The 3-acetyl-2-phenylcyclopentene (31.8g) was dissolved in methanol (250 ml), and the solution was added to a solution of potassium hydroxide (15 g) in methanol (250 ml). The reaction was monitored by g.l.c. (2% NPGS/170°) while it stood at room temperature for 24 h. After this time, the reactant had come to equilibrium with 1-acetyl-2-phenylcyclopentene, the amounts of the two isomers being approximately

equal. The solution was then poured into water (600 ml) and the product was extracted with ether, washed with water, dried and filtered. The solvent was evaporated under reduced pressure to leave a yellow oil (24.0 g), which was distilled on a Fischer Spaltrohr System distillation apparatus to give 1-acetyl-2-phenylcyclopentene⁷⁴ as required. This ketone was the more volatile of the two and was shown to be pure by g.l.c. I.r. $1620-1680\text{ cm}^{-1}$ ($\text{C}=\text{O}$ and $\text{C}=\text{C}$). $^1\text{Hn.m.r. (CDCl}_3\text{)}$: τ 2.6-2.9 (m, 5H), 7.0-7.3 (m, 4H), 7.9-8.3 (m, 2H), 8.1 (s, CH_3).

The tosylhydrazone (56%) was made by the general method, except that the reaction mixture was heated under reflux for 10 min. to complete the condensation. Recrystallisation from ethanol gave white crystals m.p. $135-136^\circ$ (d). (Found: C, 67.6; H, 6.0; N, 8.1. $\text{C}_{20}\text{H}_{22}\text{N}_2\text{SO}_2$ requires C, 67.8; H, 6.3; N, 7.9%). I.r. and $^1\text{Hn.m.r.}$ spectra: see Appendix.

4. 1-Acetyl-2-p-tolylcyclopentene was prepared by virtually the same method as the unsubstituted ketone (Ex. 3). Acetic anhydride and 1-p-tolylcyclopentene gave 3-acetyl-2-p-tolylcyclopentene (42%) b.p. $103-118^\circ/0.2\text{ mm Hg}$. $^1\text{Hn.m.r. (CDCl}_3\text{)}$: τ 2.5-3.2 (m, 4H), 3.7 (m, 1H), 6.9-7.2 (m, 1H), 7.1-8.4 (m, 4H), 7.71 (s, CH_3), 8.02 (s, CH_3). Basic isomerisation of this ketone, followed by wet column chromatography (alumina/petrol) of the crude product gave a mixture of the two ketones (20%). Distillation using the Fischer Spaltrohr System gave 1-acetyl-2-p-tolylcyclopentene (6%). (Found: m/e 200.119446. $\text{C}_{14}\text{H}_{16}\text{O}$ requires 200.120109). I.r. 1660 cm^{-1} ($\text{C}=\text{O}$). $^1\text{Hn.m.r. (CDCl}_3\text{)}$: 2.85 (s, 4H), 7.0-7.4 (m, 4H), 7.63 (s, CH_3), 7.8-8.2 (m, 2H), 8.06 (s, CH_3).

The tosylhydrazone (65%) was recrystallised from ethanol m.p. $143-144^\circ$ (d). (Found: C, 68.3; H, 6.4; N, 7.7. $\text{C}_{21}\text{H}_{24}\text{N}_2\text{SO}_2$ requires C, 68.5; H, 6.6; N, 7.6%). I.r. and $^1\text{Hn.m.r.}$ spectra: see Appendix.

5. 1-Acetyl-2-p-fluorophenylcyclopentene was prepared in collaboration with Mr. T.W. Naisby, using the same method as for the unsubstituted ketone (Ex. 3). Acetic anhydride and 1-p-fluorophenylcyclopentene gave 3-acetyl-2-p-fluorophenylcyclopentene (55%) b.p. $99-107^{\circ}/0.6$ mm Hg. $^1\text{H.N.m.r.}$ (CDCl_3): τ 2.5-3.3 (m, 4H), 3.7 (m, 1H), 5.9-6.2 (m, 1H), 7.2-8.3 (m, 4H), 7.98 (s, CH_3). Basic isomerisation of this ketone gave the usual mixture of both ketones (55%) which was distilled on the Fischer Spaltrohr System to give pure 1-acetyl-2-p-fluorophenylcyclopentene as required. (Found: C, 76.4; H, 6.4. m/e 204.094005. $\text{C}_{13}\text{H}_{13}\text{OF}$ requires C, 76.5; H, 6.4%. 204.095037). I.r. 1660 cm^{-1} ($\text{C}=\text{O}$). $^1\text{H.N.m.r.}$ (CDCl_3): τ 2.7-3.2 (m, 4H), 7.0-7.3 (m, 4H), 7.6-8.5 (m, 2H), 8.04 (s, CH_3).

The tosylhydrazone (82%) was recrystallised from ethanol m.p. $143-145^{\circ}$ (d). (Found: C, 64.8; H, 6.0; N, 7.8. $\text{C}_{20}\text{H}_{21}\text{FN}_2\text{SO}_2$ requires C, 64.5; H, 5.7; N, 7.5%). I.r. and $^1\text{H.N.m.r.}$ spectra: see Appendix.

6. 2-Phenylcyclopenten-1-al. This was prepared by an adaption of the method of Schmidle and Barnett.⁷⁵ Dimethylformamide (40 g, 0.55 mol) and phosphorus oxychloride (84.5 g, 0.55 mol) were dissolved in 1,2-dichloroethane (150 ml). The solution was stirred at 5° while 1-phenylcyclopentene (72 g, 0.5 mol) was slowly added. The solution was then heated under reflux for 15 min, then cooled and a solution of sodium acetate (278 g, 2.75 mol) in water (600 ml) was added. The resulting solution was heated under reflux for 15 min, cooled and the product was extracted with ether, washed with water, dried, filtered and the solvent was evaporated under reduced pressure to leave a brown oil (100 g). This oil was purified by wet column chromatography (alumina/petrol, ether) to give 2-phenylcyclopenten-1-al (16.2 g, 19%). (Found: C, 83.6; H, 7.3. $\text{C}_{12}\text{H}_{12}\text{O}$ requires C, 83.7; H, 7.0%). I.r. $1630-$

1680 cm^{-1} ($\text{C} = \text{O}$ and $\text{C} = \text{C}$). $^1\text{Hn.m.r.}$ (CDCl_3): τ 0.2 (s, 1H), 2.65 (s, 5H), 6.8–8.2 (m, 6H).

- 6a. 2-Phenylcyclopenten-1-al tosylhydrazone. 2-Phenylcyclopenten-1-al (12.0 g, 0.07 mol) was dissolved in ether (400 ml). Tosylhydrazide (13.0 g, 0.07 mol) was then added and the resulting mixture was shaken to dissolve as much of the solid as possible. The reaction was monitored by t.l.c. (alumina/methylene chloride), while the mixture was kept at, or below, room temperature. After 3 days no aldehyde was left and the solvent was partially evaporated under reduced pressure until 100 ml of reaction mixture remained. A yellow precipitate was then filtered off (18.8 g). This material was recrystallised from a mixture of petrol and ether to give white crystals of 2-phenylcyclopenten-1-al tosylhydrazone (14.57 g, 61%). m.p. 110–111° (d). (Found: C, 67.2; H, 6.1; N, 8.2. $\text{C}_{19}\text{H}_{20}\text{N}_2\text{SO}_2$ requires C, 67.1; H, 5.9; N, 8.2%). I.r. and $^1\text{Hn.m.r.}$ spectra: see Appendix.

7. 1-Acetyl-2-phenylcyclohexene⁷⁶ was prepared by virtually the same method as that used for 1-acetyl-2-phenylcyclopentene (Ex. 3), except that excess acetic anhydride was used as the solvent in place of carbon disulphide. 1-Phenylcyclohexene (0.15 mol) and acetic anhydride (0.375 mol) gave a crude product, which was purified by dry column chromatography (alumina/petrol) to give 3-acetyl-2-phenylcyclohexene (86%).⁷⁷ I.r. 1710 cm^{-1} ($\text{C} = \text{O}$). $^1\text{Hn.m.r.}$ (CDCl_3): τ 2.78 (s, 5H), 3.77 (m, 1H), 6.25 (m, 1H), 7.5–8.7 (m, 6H), 8.03 (s, CH_3). Basic isomerisation gave the usual mixture of ketones (74%) which was distilled by means of the Fischer Spaltrohr System to give 1-acetyl-2-phenylcyclohexene as required. (Found: C, 84.0; H, 8.3. $\text{C}_{14}\text{H}_{16}\text{O}$ requires C, 84.0; H, 8.1%). I.r. 1665 cm^{-1} ($\text{C} = \text{O}$). $^1\text{Hn.m.r.}$ (CDCl_3): τ 2.6–2.9 (m, 5H), 7.4–7.9 (m, 4H), 8.0–8.4 (m, 2H), 8.33 (s, CH_3).

The tosylhydrazone (80%) was recrystallised from ethanol. m.p. 145-146° (d). (Found: C, 68.5; H, 6.6; N, 7.7. $C_{21}H_{24}N_2SO_2$ requires C, 68.5; H, 6.6; N, 7.6%). I.r. and 1H n.m.r. spectra: see Appendix.

8. 2-Acetyl-3-phenylindene. This was prepared in collaboration with Mr. T.W. Naisby. Acetic anhydride (26.5 g, 0.26 mol) and 3-phenylindene (46.5 g, 0.24 mol) were dissolved in carbon disulphide (200 ml) and the solution was cooled to -10°. Zinc chloride (35.5 g, 0.26 mol) was added and the mixture was then stirred at room temperature for 15 h, while the reaction was monitored by g.l.c. (2% NPGS/210°). The reaction was then poured into water (500 ml), the product was extracted with ether, washed with water, dilute potassium bicarbonate solution and water again. After drying, the solvent was evaporated under reduced pressure to leave crude product (56.5 g) which was crystallised from petrol to give 2-acetyl-3-phenylindene (28.0 g, 51%) m.p. 74-74.5°. (Found: C, 87.4; H, 6.3. $C_{17}H_{14}O$ requires C, 87.2; H, 6.0%). I.r. (nujol) 1645 cm^{-1} (C = O). 1H n.m.r. ($CDCl_3$): τ 2.4-3.1 (m, 9H), 6.17 (s, CH_2), 8.01 (s, CH_3).

The tosylhydrazone (85%) was recrystallised from ethanol m.p. 204-207° (d). (Found: C, 72.0; H, 5.7; N, 7.2. $C_{24}H_{22}N_2SO_2$ requires C, 71.6; H, 5.5; N, 7.0%). I.r. and 1H n.m.r. spectra: see Appendix.

9. 2,3-Dimethylcyclohex-2-enone.⁶² This was prepared by an adaption of the method of Smith and Rouault.⁶² 4-Carboxy-3-methylcyclohex-2-enone (69 g, 0.38 mol) was dissolved in a solution of sodium (9.9 g, 0.43 mol) in rerectified ethanol (160 ml). The resulting red solution was stirred at room temperature while methyl iodide (54 g, 0.38 mol)

was added and the reaction was then stirred for 20 h, and finally heated under reflux for 2.5 h. Most of the ethanol (130 ml) was then evaporated under reduced pressure and the residue was diluted with water (220 ml). The product was extracted with ether, washed with water and the solvent evaporated under reduced pressure to leave crude 4-carbethoxy-2,3-dimethylcyclohex-2-enone (74.4 g). I.r. 1669 ($C=O$, conjugated), 1732 cm^{-1} ($C=O$, ester).

This ester (74.4 g) was dissolved in a solution of potassium hydroxide (18.3 g) in ethanol (210 ml). The resulting solution was heated under reflux for 8 h, and the solvent was then evaporated under reduced pressure. The residue was poured into water (350 ml) and the product was extracted with ether, washed with water, dried and the solvent was evaporated under reduced pressure to leave a red-brown oil (63.1 g), which was distilled to give 2,3-dimethylcyclohex-2-enone (17.6 g, 37%) b.p. $85-90^{\circ}/15\text{ mm Hg}$ (lit.,⁶² $80-84^{\circ}/9\text{ mm Hg}$). I.r.⁷⁸ 1660 ($C=O$), 1635 cm^{-1} ($C=C$). $^1\text{Hn.m.r. (CDCl}_3)$: τ 7.64 (m, 4H), 8.07 (s, CH_3), 8.05 (m, 2H), 8.23 (s, CH_3).

The tosylhydrazone (76%) was recrystallised from a mixture of methanol (1 part) and ethanol (1 part). m.p. $147-148^{\circ}$ (d). (Found: C, 61.9; H, 6.9; N, 9.8. $\text{C}_{15}\text{H}_{20}\text{N}_2\text{SO}_2$ requires C, 61.6; H, 6.9; N, 9.6%). I.r. and $^1\text{Hn.m.r.}$ spectra: see Appendix.

10. 2-(cis-Methyl-trans-phenylmethylene)cyclohexanone.⁷⁹ This was prepared by K.A. Wall,⁶⁴ using an adaption of the method of Hoffmann and Förster. Triphenyl(phenylethynyl)phosphonium bromide (30 g, 68 m mol), and 1-morpholinocyclohexene (15 g, 90 m mol) were heated under reflux for 24 h in freshly distilled acetonitrile (300 ml). The reaction was monitored by t.l.c. (alumina/ethanol) until no starting material remained. The solvent was then evaporated under reduced pressure to leave a brown

oil. A solution of sodium hydroxide (60 g) in water (300 ml) was added to this oil and the mixture was heated under reflux in an atmosphere of nitrogen for 2 days. The product was then extracted with ether and the ether was evaporated under reduced pressure. Dilute hydrochloric acid (300 ml) was added to the residue and the mixture was stirred at room temperature for 18 h. The product was extracted with ether, dried and the solvent was evaporated under reduced pressure. The crude product was distilled to give 2-(cis-methyl-trans-phenylmethylene)cyclohexanone (6.5 g, 48%). b.p. $130^{\circ}/2$ mm Hg (lit.,⁷⁹ $159^{\circ}/11$ mm Hg). I.r. 1690 cm^{-1} ($\text{C}=\text{O}$). $^1\text{H.n.m.r.}$ (CDCl_3): τ 2.5-3.1 (m, 5H), 7.3-8.5 (m, 8H), 7.82 (s, CH_3).

The tosylhydrazone (62%) was prepared by Mr. K.A. Wall,⁶⁴ using the general method. A sample of the product was recrystallised from ethanol. m.p. $136-140^{\circ}$. (Found: C, 68.2; H, 6.5; N, 7.5. $\text{C}_{21}\text{H}_{24}\text{N}_2\text{SO}_2$ requires C, 68.5; H, 6.6; N, 7.6%). I.r. and $^1\text{H.n.m.r.}$ spectra: see Appendix.

11. 2-(Di-p-tolylmethylene)cyclohexanone. This was prepared in collaboration with Mr. T.W. Naisby, using an adaption of the method of Thorogood.⁴⁰ Magnesium (5.6 g, 0.23 mol) and ether (40 ml) were stirred under nitrogen at room temperature. A crystal of iodine was added and a portion of a solution of p-bromotoluene (32 g, 0.19 mol) in ether (120 ml) was run in. After the reaction had started, the remainder of the solution was slowly added, and the reaction was driven to completion by heating under reflux for 20 min. The mixture was then cooled to 0° and a solution of 2-ethylenedioxyethoxycarbonylcyclohexane (20 g, 0.094 mol) in ether (30 ml) was added dropwise, with stirring. The reaction was stirred for 15 h, then heated under reflux for 1 h. After cooling, the complex was decomposed by the cautious addition of a solution of ammonium

chloride (70 g) in water (350 ml). The product was extracted with ether, washed with water and the solvent was evaporated under reduced pressure to leave crude di-p-tolyl(2-ethylenedioxcyclohexyl)methanol (24.7 g), a yellow oil which solidified on cooling. Hydrolysis and dehydration of this alcohol were carried out by heating it under reflux in a mixture of methanol (135 ml), water (90 ml) and concentrated hydrochloric acid (4 ml) for 4 h. Examination by g.l.c. (5% NPGS/160°) then showed that nearly all the reactants had been used up. On cooling, a yellow solid separated and it was filtered off. A further crop of product was crystallised from ethanol and the combined material was recrystallised from ethanol to give yellow crystals of 2-(di-p-tolylmethylene)cyclohexanone (4.1 g, 16%) m.p. 139-141° (lit.,⁴⁰ 149°).

The tosylhydrazone (89%) was recrystallised from ethanol. m.p. 163-164° (d) (lit.,⁴⁰ 159° (d)).

PREPARATION AND DECOMPOSITION OF THE SODIUM
SALTS OF THE TOSYLHYDRAZONES, AND RELATED REACTIONS.

General Method of Preparation and Decomposition of the Tosylhydrazone
Sodium Salts.

The sodium salts were prepared by the addition of the tosylhydrazone to an equimolar quantity of sodium dissolved in super-dry ethanol, under dry nitrogen, in the dark. In most cases, a very slight excess of the tosylhydrazone (1-2%) was used to ensure that no excess sodium was present to cause base-catalysed reactions. In some cases, the tosylhydrazone was added in solution, either in a minimum of dry ethanol, or in dry DME. The mixture was stirred until all the tosylhydrazone had dissolved. In some cases, the sodium salt precipitated at this stage. The solvents were then evaporated under reduced pressure (0.1 mm or 10 mm Hg) and anhydrous conditions, always keeping the temperature below 35°. The sodium salts were then dried under high vacuum for at least 12 h. The reaction solvent, usually cyclohexane or DME, was then added and the mixture heated under reflux under nitrogen in the dark. During the decompositions, small samples (0.1 ml) of the reaction mixture were withdrawn and plunged into either water or dilute hydrochloric acid in order to hydrolyse any residual sodium salt. Any tosylhydrazone so formed was extracted with ether, and its presence detected by t.l.c. comparison with an authentic sample. The reaction was continued until all the starting material had been consumed. The reactions were usually worked up by filtering off the precipitated sodium *p*-toluenesulphinate and evaporating the filtrate to give the product.

1. 1-Benzoyl-2-phenylcyclopentene tosylhydrazone.⁴³

- a) Decomposition in Cyclohexane. The sodium salt of 1-benzoyl-2-phenylcyclopentene tosylhydrazone (659 mg, 1.58 mmol) was heated

under reflux in cyclohexane (25 ml) for 20 h. After 15 min the reaction was mauve, but this gradually faded to a cream colour. The usual work up gave a yellow solid, 1,2,3,4-tetrahydro-4-phenylcyclopenta[b]indene (348 mg, 95%). This material was sublimed under high vacuum to give white crystals. m.p. 57-58°. (Found: C, 93.1; H, 6.7. $C_{18}H_{16}$ requires C, 93.1; H, 6.9%). 1H N.m.r. and mass spectra: see Appendix.

b) Decomposition in Cyclohexane in the Presence of 1,1-Diphenylethylene.

A mixture of 1-benzoyl-2-phenylcyclopentene tosylhydrazone (1.36 g, 3.26 m mol) sodium salt and 1,1-diphenylethylene (5.05 g, 28.0 m mol) in cyclohexane (10 ml) was heated under reflux for 20 h. G.l.c. (1% SE 30/170-250°) and t.l.c. (alumina/petrol) showed that the only product was 1,2,3,4-tetrahydro-4-phenylcyclopenta[b]indene.

c) Hydrogenation of 1,2,3,4-Tetrahydro-4-phenylcyclopenta[b]indene.⁴³

10% Palladium on charcoal (97 mg), concentrated hydrochloric acid (2 drops) and 1,2,3,4-tetrahydro-4-phenylcyclopenta[b]indene (147 mg, 0.634 m mol) were added to ethanol (30 ml). The mixture was shaken in a Parr hydrogenator under a pressure of 4 atmospheres of hydrogen for 1 h. After this time, g.l.c. (2½% OVI/200°) showed that no reactant remained and that only one product had formed. G.l.c.-m.s. showed that this product had a molecular ion of 234. The catalyst was filtered off through a pad of celite and the ethanol was evaporated under reduced pressure to leave 4-phenylcyclopenta[a]indane (130 mg, 88%). 1H N.m.r. spectrum: see Appendix, identical with reported spectrum.⁸⁰

2. 1-Acetyl-2-methylcyclopentene tosylhydrazone.⁴³

a) Decomposition in Cyclohexane. The sodium salt of 1-acetyl-2-methylcyclopentene tosylhydrazone (1.087 g, 3.72 m mol) was heated

under reflux in cyclohexane (10 ml) for 19h. During the decomposition, the mixture quickly became a deep violet colour which slowly faded to yellow. After the usual work up, t.l.c. (alumina/methylene chloride) and g.l.c. (1% SE 30) both indicated the formation of multiple products, which, from their Rf values, appeared to be hydrocarbons. This agreed with the results of Stanley.⁴³

b) Decomposition in Cyclohexane in the Presence of 1,1-Diphenylethylene.

A mixture of 1-acetyl-2-methylcyclopentene tosylhydrazone (3.17 g, 10.85 m mol) sodium salt and 1,1-diphenylethylene (11.2 g, 62.3 m mol) in cyclohexane (25 ml) was heated under reflux for 20 h. The usual work up gave a yellow liquid (12.38 g) which was shown by g.l.c. (1% SE 30/130-170⁰) to contain 1,1-diphenylethylene and one other component. The liquid was then distilled under high vacuum to remove the 1,1-diphenylethylene and the residue was separated by dry column chromatography (alumina/ petrol) to give 1-methyl-2-(1-methyl-2,2-diphenylcyclopropyl)cyclopentene (1.33 g, 44%). (Found: C, 91.9; H, 8.1. m/e 288.186006. C₂₂H₂₄ requires C, 91.6; H, 8.4%. m/e 288.187792). ¹HN.m.r. and mass spectra: see Appendix.

c) Decomposition in Cyclohexene.⁴³ The sodium salt of 1-acetyl-2-methylcyclopentene tosylhydrazone (1.01 g, 3.45 m mol) was heated under reflux in freshly distilled cyclohexene (30 ml) for 19 h. The usual work up gave a yellow filtrate, which, on examination by t.l.c., showed multiple products. G.l.c. (1% SE 30/90-200⁰) also illustrated the presence of many products. G.l.c.- mass spectra were run on the largest of the peaks, but none of these spectra had molecular ions of 190 which would have indicated addition of the carbene to cyclohexene. This result is in agreement with Stanley.⁴³

- d) Hydrogenation of 1-Methyl-2-(1-methyl-2,2-diphenylcyclopropyl)-cyclopentene. Ethanol (22 ml) containing 10% palladium on charcoal (60 mg) was shaken in an atmosphere of hydrogen to saturate the solvent with gas. 1-Methyl-2-(1-methyl-2,2-diphenylcyclopropyl)cyclopentene (68 mg, 0.235 m mol) in ethanol (2 ml) was then added, and the mixture was hydrogenated at atmospheric pressure for 17 h. A total of 9.6 ml of hydrogen was consumed. G.l.c. (1% SE 30/160⁰) showed that the solution still contained about 5% of reactant as well as two major products and three minor ones. The reaction was driven to completion by hydrogenation for 26 h at 4 atmospheres in a Parr hydrogenator, using additional 10% palladium on charcoal (30 mg). G.l.c. indicated that no new products had been formed. The catalyst was removed by filtration through a celite pad and the solvent was evaporated under reduced pressure to leave a colourless oil (44 mg, 64%) which could not be separated into its components. (Found: m/e 292.219005. C₂₂H₂₈ requires 292.219090). ¹H.N.m.r. and mass spectra: see Appendix.

3. 1-Acetyl-2-phenylcyclopentene tosylhydrazone.

- a) Decomposition in 1,2-Dimethoxyethane. The sodium salt of 1-acetyl-2-phenylcyclopentene tosylhydrazone (2.89 g, 8.15 m mol) was heated under reflux in DME (50 ml) for 9 h. The usual work up gave a brown oil which was shown by t.l.c. (alumina/petrol) to contain three components, at R_f 0.9, R_f 0.2 and R_f 0.1. These components were separated by dry column chromatography (alumina/petrol) to give 1,2,3,4-tetrahydro-4-methylcyclopenta[b]indene (271 mg, 20%), 1,2,3,4-tetrahydro-4-methylbenzo[c]cyclopenta[e]-[1,2]-diazepine (520 mg, 32%) and 4,5,6-trihydro-3-methyl-6a-phenylcyclopenta[c]pyrazole (740 mg, 46%). The indene was shown to be pure by g.l.c. (1% SE 30/110⁰) and t.l.c. (alumina/petrol). I.r. (liquid) 1630 cm⁻¹ (C = C). (Found: m/e 170.109216. C₁₃H₁₄ requires 170.109545). ¹H.N.m.r. and mass spectra: see Appendix.

The yellow diazepine oil was purified by wet column chromatography (alumina/petrol, methylene chloride) and then by crystallisation from petroleum/ether (10:1) m.p. 50-52°. (Found: C, 78.5; H, 7.1; N, 14.0. m/e 198.114706, 170.109384. $C_{13}H_{14}N_2$ requires C, 78.8; H, 7.1; N, 14.1% m/e 198.115693. $C_{13}H_{14}$ requires 170.109545). U.v., 1H n.m.r., ^{13}C n.m.r. and mass spectra: see Appendix.

The pyrazole was purified by dry column chromatography (alumina/ether) to give a colourless oil. (Found: C, 78.8; H, 7.4; N, 13.9. m/e 198.115902, 170.109384. $C_{13}H_{14}N_2$ requires C, 78.9; H, 7.1; N, 14.1%. m/e 198.115693. $C_{13}H_{14}$ requires 170.109545). U.v., 1H n.m.r., ^{13}C n.m.r. and mass spectra: see Appendix.

- b) Decomposition in DME, Monitored by H.S.L.C. The sodium salt of 1-acetyl-2-phenylcyclopentene tosylhydrazone (1.39 g, 3.93 mmol) was heated under reflux in DME (20 ml). At regular intervals a sample of the solution was removed by syringe and examined directly by h.s.l.c. (alumina/methylene chloride). The production of 1,2,3,4-tetrahydro-4-methylbenzo[c]cyclopenta[e]-[1,2]-diazepine and 4,5,6-trihydro-3-methyl-6a-phenylcyclopenta[c]pyrazole was observed, using the ultraviolet detector at 258 nm (diazepine, ϵ 9290; pyrazole, ϵ 2360).

Table 1.

The Ratio of the Number of Moles of Diazepine to the Number of Moles of Pyrazole in Solution

| Time (h) | Diazepine / Pyrazole |
|----------|----------------------|
| 0.50 | 8 / 92 |
| 1.50 | 8 / 92 |
| 2.75 | 12 / 88 |
| 5.00 | 20 / 80 |

c) Decomposition in DME in the Presence of Tri-n-butylphosphine.

The sodium salt of 1-acetyl-2-phenylcyclopentene tosylhydrazone (1.60 g, 4.5 m mol) and tri-n-butylphosphine (1.82 g, 9.0 m mol) were heated under reflux in DME (20 ml) for 9 h. The usual work up gave a yellow-brown solution. H.s.l.c. (alumina/methylene chloride) showed the absence of the usual heterocyclic products. The reaction solvent was evaporated under reduced pressure and dry column chromatography (alumina/ether) of the resulting oil gave 1-acetyl-2-phenylcyclopentene hydrazone (637 mg, 71%), which was recrystallised from a mixture of petrol, b.p. 60-80° (6 parts) and ethanol (1 part) to give cream coloured diamond shaped crystals. m.p. 102-103°. (Found: C, 77.8; H, 8.2; N, 13.9. $C_{13}H_{16}N_2$ requires C, 78.0; H, 8.1; N, 14.0%). I.r. (nujol): 3365, 3280, 3215 cm^{-1} (all N-H). $^1HN.m.r.$ ($CDCl_3$): τ 2.8 (s, 5H), 4.8-4.9 (bs, NH_2), 7.0-7.4 (m, 4H), 7.8-8.3 (m, 2H), 8.48 (s, CH_3).

d) Condensation of 1-Acetyl-2-phenylcyclopentene hydrazone with Acetone.

1-Acetyl-2-phenylcyclopentene hydrazone (62 mg) was dissolved in acetone (2 ml). The excess acetone was evaporated by boiling the solution at atmospheric pressure to leave the azine as a yellow oil. (Found: m/e 240.160831. $C_{16}H_{20}H_2$ requires 240.162641). $^1HN.m.r.$ ($CDCl_3$): τ 2.8 (s, 5H), 6.9-7.3 (m, 4H), 7.7-8.2 (m, 2H), 8.00 (s, CH_3), 8.20 (s, CH_3), 8.36 (s, CH_3). Mass spectrum: m/e 240 (64), 239 (100), 184 (21), 182 (29).

e) Decomposition of 4,5,6-Trihydro-3-methyl-6a-phenylcyclopenta[c]-

pyrazole in DME. The pyrazole (161 mg, 0.81 m mol) was heated under reflux, in the dark, under nitrogen, in DME (20 ml). The colourless solution became yellow after a few minutes and the colour intensified as the reaction progressed. Examination by t.l.c. (alumina/toluene) during 23 h showed the disappearance of reactant and the appearance



of 1,2,3,4-tetrahydro-4-methylcyclopenta[b]indene and 1,2,3,4-tetrahydro-4-methylbenzo[c]cyclopenta[e]-[1,2]-diazepine. The solution was cooled and the solvent was evaporated under reduced pressure to leave a yellow oil. ^1H .n.m.r. spectroscopy indicated that the ratio of indene to diazepine was approximately 2:1. H.s.l.c. (alumina/methylene chloride), using the ultraviolet detector at 258 nm (indene, ϵ 6400; diazepine, ϵ 9290) indicated indene (69%) and diazepine (31%) of the mixture. The products were separated by dry column chromatography (alumina/toluene) to give 1,2,3,4-tetrahydro-4-methylcyclopenta[b]indene (56 mg, 41%) which was compared with an authentic sample using t.l.c. (alumina/toluene), g.l.c. (1% SE 30/116 $^\circ$) and i.r. spectroscopy, and 1,2,3,4-tetrahydro-4-methylbenzo[c]cyclopenta[e]-[1,2]-diazepine (50 mg, 31%), which was compared with an authentic sample using t.l.c. (alumina/toluene), i.r. and u.v. spectroscopy. A brown oil (32 mg), washed off the dry column, had an R_f 0.0; this was not present before chromatography (t.l.c.).

- f) Decomposition of 4,5,6-Trihydro-3-methyl-6a-phenylcyclopenta[c]-pyrazole in DME in the Presence of Tri-n-butylphosphine. The pyrazole (225 mg, 1.14 m mol) and tri-n-butylphosphine (445 mg, 2.25 m mol) were dissolved in DME (5 ml), and the solution was heated under reflux in the dark under nitrogen. The reaction was monitored by h.s.l.c. (alumina/methylene chloride: n-hexane, 1:1), which showed that no reactant remained after 4.25 h. H.s.l.c. also indicated that neither 1,2,3,4-tetrahydro-4-methylcyclopenta[b]-indene nor 1,2,3,4-tetrahydro-4-methylbenzo[c]cyclopenta[e]-[1,2]-diazepine had been formed in the reaction. The mixture was cooled and the solvent evaporated under reduced pressure. Dry column chromatography (alumina/ether) of the residue, followed by crystallisation from petrol gave 1-acetyl-2-phenylcyclopentene hydrazone

(139 mg, 61%). $^1\text{HN.m.r.}$: identical with previous sample.

- g) Attempted Decomposition of 1,2,3,4-Tetrahydro-4-methylbenzo[c]cyclopenta[e]-[1,2]-diazepine in DME in the Presence of Tri-n-butylphosphine. The diazepine (45 mg, 0.23 m mol) and tri-n-butylphosphine (91 mg, 0.45 m mol) were dissolved in DME (1 ml) and the solution was heated under reflux in the dark under nitrogen for 9 h. The mixture was then cooled and water (1 drop) was added to ensure the hydrolysis of any adduct which had been formed. T.l.c. (alumina/benzene) showed that no 1-acetyl-2-phenylcyclopentene hydrazone had been formed. The diazepine (43 mg) was recovered, using wet column chromatography (alumina/petrol, methylene chloride).
- h) Attempted Decomposition of 1,2,3,4-Tetrahydro-4-methylbenzo[c]cyclopenta[e]-[1,2]-diazepine in DME. The diazepine (18.5 mg, 0.093 m mol) was heated under reflux in DME (10 ml) in the dark under nitrogen for 9 h. Examination by t.l.c. (alumina/toluene) showed that no reaction had taken place. The solution was then cooled and sodium p-toluenesulphinate (16.6 mg, 0.093 m mol) was added. The mixture was then heated under reflux, in the dark under nitrogen for a further 16 h. Examination by t.l.c. again showed that no reaction had taken place.
- i) Gas Phase Pyrolysis of 1,2,3,4-Tetrahydro-4-methylbenzo[c]cyclopenta[e]-[1,2]-diazepine. A vacuum pyrolysis furnace was heated to 400° at a pressure of 0.1 mm Hg. The inlet tube containing 1,2,3,4-tetrahydro-4-methylbenzo[c]cyclopenta[e]-[1,2]-diazepine (108 mg, 0.55 m mol) was slowly heated to 100° in order to vaporise the reactant which then passed through the furnace; the products being collected in a trap cooled by liquid nitrogen. After 24 h, no reactant was left and a pale yellow liquid (110 mg) had gathered in the trap. T.l.c. (alumina/petrol) indicated that this liquid

contained no reactant. G.l.c. (1% SE 30/89⁰) showed the presence of 2 compounds, with peak areas in the ratio of 2:1. The more abundant material had a retention time equal to that of 1,2,3,4-tetrahydro-4-methylcyclopenta[b]indene. G.l.c.- m.s. (5% Carbowax/150⁰) indicated that both components had identical mass spectra to the above indene. Dry column chromatography (alumina/petrol) of the crude product gave a mixture of 1,2,3,4-tetrahydro-4-methylcyclopenta[b]indene and 1,2,3,8b-tetrahydro-4-methylcyclopenta[a]-indene (66 mg, 71%). ¹H.N.m.r. (CDCl₃): τ 2.6-3.1 (m, 4H), 6.3-7.0 (m, 1H), 7.2-7.9 (m, 6H), 8.00 bs, 1/3CH₃, 8.72 (d, J 7Hz, 2/3CH₃).

j) Hydrogenation of 1,2,3,4-Tetrahydro-4-methylcyclopenta[b]indene.

10% Palladium on charcoal (93 mg) and 1,2,3,4-tetrahydro-4-methylcyclopenta[b]indene (141 mg, 0.83 mmol) were added to ethanol (30 ml) and the mixture was shaken in a Parr hydrogenator under a pressure of 4 atmospheres for 50 min. G.l.c. and g.l.c.- m.s. (1% SE 30/110⁰) indicated that all the reactant had been consumed and two isomeric products (ratio 8:1) had been formed. The catalyst was removed by filtration through celite and the solvent was evaporated under reduced pressure to leave a colourless oil (78 mg, 55%) which was distilled under high vacuum to give 4-methylcyclopenta[a]indane (57 mg, 41%). (Found: m/e 172.125083. C₁₃H₁₆ requires 172.125194). ¹H.N.m.r. spectrum: see Appendix.

4. 1-Acetyl-2-p-tolylcyclopentene tosylhydrazone.

- a) Decomposition in DME. The sodium salt of 1-acetyl-2-p-tolylcyclopentene tosylhydrazone (2.25 g, 6.12 mmol) was heated under reflux in DME (40 ml) for 4 h. The usual work up, followed by wet column chromatography (alumina/petrol) of the residue gave 1,2,3,4-tetrahydro-4,6-dimethylcyclopenta[b]indene (219 mg, 20%), 1,2,3,4-tetra-

hydro-4,8-dimethylbenzo[c]cyclopenta[e]-[1,2]- diazepine (472 mg, 37%) and 4,5,6-trihydro-3-methyl-6a-p-tolylcyclopenta[c]pyrazole (553 mg, 43%).

The indene was shown to be pure by t.l.c. (alumina/petrol). (Found: m/e 184.124632. $C_{14}H_{16}$ requires 184.125194). 1H n.m.r. and mass spectra: see Appendix.

The diazepine was purified by wet column chromatography (alumina/petrol, ether) to give yellow crystals (265 mg) which were recrystallised from petrol. m.p. 89-90°. (Found: C, 79.3; H, 7.9; N, 13.6. m/e 212.130878, 184.124994. $C_{14}H_{16}N_2$ requires C, 79.2; H, 7.6; N, 13.2%. m/e 212.131342. $C_{14}H_{16}$ requires 184.125194). U.v., 1H n.m.r., ^{13}C n.m.r. and mass spectra: see Appendix.

The pyrazole was purified by wet column chromatography (alumina/ether) to give a pale brown oil (394 mg). (Found: m/e 212.131085, 184.124994. $C_{14}H_{16}N_2$ requires 212.131342. $C_{14}H_{16}$ requires 184.125194). U.v., 1H n.m.r., ^{13}C n.m.r. and mass spectra: see Appendix.

- b) Decomposition of 4,5,6-Trihydro-3-methyl-6a-p-tolylcyclopenta[c]-pyrazole in DME. The pyrazole (182 mg, 0.86 m mol) was heated under reflux in DME (15 ml) in the dark under nitrogen for 18 h, when t.l.c. (alumina/methylene chloride) showed that no reactant remained. The solution was cooled and the solvent was evaporated under reduced pressure. Dry column chromatography (alumina/benzene), (alumina/petrol) of the residual yellow oil gave 1,2,3,4-tetrahydro-4,6-dimethylcyclopenta[b]indene (55 mg, 35%) which was identical with an authentic sample using t.l.c. (alumina/petrol), g.l.c. (1% SE 30/120°) and 1H n.m.r. spectroscopy; and 1,2,3,4-tetrahydro-4,6-dimethylbenzo[c]cyclopenta[e]-[1,2]- diazepine (67 mg, 37%), 1H n.m.r. ($CDCl_3$) identical with that of an authentic sample. A

brown oil (18 mg, 10%) was also collected from the benzene dry column (Rf 0.0). Such material had not been present before chromatography (t.l.c.).

5. 1-Acetyl-2-p-fluorophenylcyclopentene tosylhydrazone.

- a) Decomposition in DME. The sodium salt of 1-acetyl-2-p-fluorophenylcyclopentene tosylhydrazone (3.25 g, 8.72 m mol) was heated under reflux in DME (40 ml) for 6 h. The usual work up gave an orange oil (1.87 g). Dry column chromatography (alumina/petrol) gave 6-fluoro-1,2,3,4-tetrahydro-4-methylcyclopenta[b]indene (443 mg, 27%), 8-fluoro-1,2,3,4-tetrahydro-4-methylbenzo[c]cyclopenta[e]-[1,2]-diazepine (709 mg, 38%) and 6a-p-fluorophenyl-4,5,6-trihydro-3-methylcyclopenta[c]pyrazole (678 mg, 36%).

The indene was shown to be pure by t.l.c. (alumina/petrol). (Found: m/e 188.099147. $C_{13}H_{13}F$ requires 188.100122). $^1Hn.m.r.$ and mass spectra: see Appendix.

The diazepine was shown to be pure by t.l.c. (alumina/benzene). Crystallisation from a mixture of petrol (10 parts) and ether (1 part) gave yellow needles m.p. 80-81°. (Found: C, 72.0; H, 6.3; N, 13.1. $C_{13}H_{13}N_2F$ requires C, 72.2; H, 6.1; N, 13.0%). U.v., $^1Hn.m.r.$, $^{13}Cn.m.r.$ and mass spectra: see Appendix.

The pyrazole was shown to be pure by t.l.c. (alumina/benzene). (Found: m/e 216.106012, 188.100414. $C_{13}H_{13}N_2F$ requires 216.106269, $C_{13}H_{13}F$ requires 188.100122). U.v., $^1Hn.m.r.$, $^{13}Cn.m.r.$ and mass spectra: see Appendix.

- b) Decomposition of 6a-p-Fluorophenyl-4,5,6-trihydro-3-methylcyclopenta[c]pyrazole in DME. The pyrazole (403 mg, 1.86 m mol) was dissolved in dry DME (15 ml) and the solution was heated under reflux in the dark under nitrogen. The reaction was monitored by

t.l.c. (alumina/methylene chloride, petrol) which showed no significant quantity of reactant left after heating for 12 h. The reaction was cooled and the solvent was evaporated under reduced pressure to leave a yellow oil. Dry column chromatography (alumina/benzene) gave 6-fluoro-1,2,3,4-tetrahydro-4-methylcyclopenta[b]indene (85 mg, 24%), 8-fluoro-1,2,3,4-tetrahydro-4-methylbenzo[c]cyclopenta[e]-[1,2]-diazepine (126 mg, 33%), both of which had $^1\text{Hn.m.r.}$ spectra identical with authentic samples and a brown oil (95 mg), R_f 0.0-0.1, which was shown by $^1\text{Hn.m.r.}$ spectroscopy to contain some residual reactant (10% approx. of the original quantity), as well as unidentifiable material.

6. 2-Phenylcyclopenten-1-al tosylhydrazone.

- a) Decomposition in DME. The sodium salt of 2-phenylcyclopenten-1-al tosylhydrazone (2.45 g, 7.20 mmol) was heated under reflux in DME (40 ml) for 4 h during which time a red coloration appeared, then faded. The usual work up gave a brown oil (1.47 g) which was separated by dry column chromatography (alumina/petrol) into two fractions, with $R_f > 0.7$ (388 mg) and $R_f < 0.3$ (955 mg). The fast running fraction contained at least 2 components, one of which fluoresced under ultraviolet radiation. G.l.c. (2% NPGS/200 $^\circ$) of this fraction showed 2 peaks, in the ratio 6:1. G.l.c.-m.s. of the major peak showed M^+ 156 which could be due to 1,2,3,4,4-penta-hydrocyclopenta[b]indene, however, $^1\text{Hn.m.r.}$ of the fraction could not confirm the presence of this compound. Mass spectrum: m/e 172 (25), 156 (100), 155 (44), 144 (30), 141 (37), 128 (79). (Found: 156.094119. $\text{C}_{12}\text{H}_{12}$ requires 156.093896). The slow running fraction from the dry column was added to ether. This encouraged crystallisation of 2-phenylcyclopentene-1-al azine

(59 mg, 5%). Recrystallisation from benzene gave yellow needles m.p. 205–206° (d). (Found: C, 84.8; H, 7.2; N, 8.5. $C_{24}H_{24}N_2$ requires C, 84.7; H, 7.1; N, 8.2%). 1H N.m.r. ($CDCl_3$): τ 1.54 (s, 2H), 2.6–2.8 (m, 10H), 7.1 (m, 8H), 8.0 (m, 4H). Mass spectrum: m/e 341 (24), 340 (100), 339 (65), 290 (95), 172 (76), 170 (95), 168 (65). T.l.c. (alumina/benzene and silica/benzene) of the remainder of this fraction indicated multiple products, none of which had a yellow colour, and mass spectrometry showed that peaks at 184 ($C_{12}H_{12}N_2$) and 156 ($C_{12}H_{12}$) were not outstanding.

7. 1-Acetyl-2-phenylcyclohexene tosylhydrazone.

- a) Decomposition in DME. The sodium salt of 1-acetyl-2-phenylcyclohexene tosylhydrazone (3.90 g, 10.6 mmol) was heated under reflux in DME (70 ml) for 4 h. The usual work up gave a pale brown oil which gave one spot on a t.l.c. plate (alumina/methylene chloride) and one peak (>95% of total area of peaks) on a h.s.l.c. trace (alumina/methylene chloride, hexane). Wet column chromatography (alumina/methylene chloride) followed by recrystallisation from a mixture of petrol and ethanol gave 4,5,6,7-tetrahydro-3-methyl-7a-phenylindazole (750 mg, 33%). m.p. 66–67°. (Found: C, 78.9; H, 7.7; N, 13.2. m/e 212.131085, 184.124813. $C_{14}H_{16}N_2$ requires C, 79.2; H, 7.6; N, 13.2%. m/e 212.131342. $C_{14}H_{16}$ requires 184.125194). 1H N.m.r., ^{13}C n.m.r. and mass spectra: see Appendix.
- b) Decomposition of 4,5,6,7-Tetrahydro-3-methyl-7a-phenylindazole in DME. The indazole (563 mg, 2.65 mmol) was dissolved in DME (50 ml) and the solution was heated under reflux in the dark under nitrogen for 5 days. The reaction was monitored by t.l.c. and h.s.l.c. (both using alumina/methylene chloride). Both appeared to show a small amount of reactant still left after 5 days, but as

this material did not decompose when the reaction mixture was heated under reflux in toluene for 8 h, it clearly was not reactant.

The solvent was then evaporated under reduced pressure to leave a brown oil, which on dry column chromatography (alumina/methylene chloride) gave 3-methyl-5-phenylpyrazole-4-spirocyclopentane (539 mg, 95%). This oil was sublimed under high vacuum to give white crystals of the pyrazole m.p. 62-64°. (Found: C, 79.1; H, 7.9; N, 13.3. m/e 212.130464, 184.125356 (12 parts), 184.099656 (1 part). $C_{14}H_{16}N_2$ requires C, 79.2; H, 7.6; N, 13.2%. m/e 212.131342. $C_{14}H_{16}$ requires 184.125194. $C_{12}H_{12}N_2$ requires 184.100043). 1H N.m.r., ^{13}C n.m.r. and mass spectra: see Appendix.

- c) Decomposition of 4,5,6,7-Tetrahydro-3-methyl-7a-phenylindazole in DME in the Presence of Tri-n-butylphosphine. The indazole (208 mg, 0.98 m mol) and tri-n-butylphosphine (396 mg, 1.96 m mol) were dissolved in DME and the solution was heated under reflux in the dark under nitrogen. The reaction was monitored by t.l.c. (alumina/methylene chloride), which showed the gradual disappearance of the reactant, until after 5 days, no significant quantity was left. The mixture was then cooled and the solvent was evaporated under reduced pressure. Dry column chromatography (alumina/methylene chloride) of the residue gave 3-methyl-5-phenylpyrazole-4-spirocyclopentane (194 mg, 50%), identical with an authentic sample (1H n.m.r. and t.l.c.), and a brown oil (22 mg) which did not contain 1-acetyl-2-phenylcyclohexene hydrazone.

8. 2-Acetyl-3-phenylindene tosylhydrazone.

- a) Decomposition in DME. The sodium salt of 2-acetyl-3-phenylindene tosylhydrazone (2.33 g, 5.81 m mol) was heated under reflux in DME (30 ml). After being heated for 2 min, the colourless solution

became red-brown. This colour slowly faded to leave a yellow solution after 30 min. T.l.c. (alumina/methylene chloride) showed that no reactant remained after 50 min, but the mixture was left at 65° for a further 18 h to ensure reaction of any diazoalkene. The mixture was then cooled and sodium *p*-toluenesulphinate (100%) was filtered off. The solvent was evaporated under reduced pressure to leave a solid (1.40 g) which on dry column chromatography (alumina/petrol) gave 1-methylindeno (2',3': 2,3) indene (918 mg, 72%). Recrystallisation from petrol gave white crystals m.p. 112–112.5° (Found: C, 93.7; H, 6.4. C₁₇H₁₄ requires C, 93.6; H, 6.5%). ¹H_N.m.r. (CDCl₃): τ 2.2–3.0 (m, 8H), 6.33 (q, J 8Hz, 1H), 6.45 (s, 2H), 8.58 (d, J 8Hz, CH₃). The residue from the dry column (332 mg, R_f < 0.2) showed a number of spots on a t.l.c. plate (alumina/methylene chloride), but no evidence could be found for the presence of a pyrazole or a diazepine.

9. 2,3-Dimethylcyclohex-2-enone tosylhydrazone.

- a) Decomposition in Cyclohexane. The sodium salt of 2,3-dimethylcyclohex-2-enone tosylhydrazone (1.06 g, 3.64 mmol) was heated under reflux in cyclohexane (10 ml) for 88 h. At no stage of the decomposition did any red coloration develop. After the sodium *p*-toluenesulphinate had been filtered off, t.l.c. (alumina/methylene chloride, alumina/benzene) and g.l.c. (2% NPGS/60–180°, 10% APL/80–200°) of the filtrate indicated multiple products. G.l.c.-mass spectra were run on the 3 largest peaks: 108 (38), 93 (100), 91 (63), 77 (53) – probably 1,2-dimethylcyclohexa-1,3-diene; 154 (33), 139 (81), 111 (100), 109 (33); and 192 (5), 110 (18), 109 (100), 108 (19) – probably an insertion product of the carbene into cyclohexane. The products could not be separated.

b) Decomposition in Cyclohexane in the Presence of 1,1-Diphenylethylene.

The sodium salt of 2,3-dimethylcyclohex-2-enone tosylhydrazone (1.95 g, 6.67 m mol) and 1,1-diphenylethylene (7.6 g, 42.3 m mol) were heated under reflux in cyclohexane (20 ml) for 68 h. After the sodium *p*-toluenesulphinate had been filtered off, g.l.c. and g.l.c.- m.s. (10% APL/80-200⁰) of the filtrate showed two significant products, with molecular ions 154 (identical spectrum to the compound in Ex 9a)) and 288. The solvent was evaporated under reduced pressure and dry column chromatography (alumina/petrol) of the residue followed by distillation under high vacuum gave 2,3-dimethylcyclohex-2-enespiro-2',2'-diphenylcyclopropane (353 mg, 19%) as a colourless liquid. (Found: C, 91.9; H, 8.5. C₂₂H₂₄ requires C, 91.6; H, 8.4%). ¹Hn.m.r. and mass spectra: see Appendix.

- c) Hydrogenation of 2,3-Dimethylcyclohex-2-enespiro-2',2'-diphenylcyclopropane. 10% Palladium on charcoal (50 mg) and 2,3-dimethylcyclohex-2-enespiro-2',2'-diphenylcyclopropane (57 mg, 0.20 m mol) were added to ethanol (30 ml). The mixture was shaken for 8 h under 4 atmospheres of hydrogen, when examination by g.l.c. (1% SE 30/170⁰) showed that all the reactant had been consumed. Only one product peak was seen on the g.l.c. trace and g.l.c.- m.s. indicated M+292. (Found: m/e 292.218206. C₂₂H₂₈ requires 292.219090). ¹Hn.m.r. and mass spectrum: see Appendix.

10. 2-(cis-Methyl-trans-phenylmethylene)cyclohexanone tosylhydrazone.

- a) Decomposition in DME. The sodium salt of 2-(cis-methyl-trans-phenylmethylene) cyclohexanone tosylhydrazone (2.42 g, 6.57 m mol) was heated under reflux in DME (50 ml) for 30 h. T.l.c. (alumina/methylene chloride) of the product indicated the formation of only one product. The usual work up, then wet column chromatography

(alumina/methylene chloride) of the product, followed by recrystallisation from a mixture of petrol and ethanol, gave 4,5,6,7-tetrahydro-3-methyl-3-phenylindazole (807 mg, 58%) m.p. 64-65°.

(Found: C, 79.3; H, 7.2; N, 13.2. m/e 212.129843, 184.124813 (10 parts), 184.099837 (1 part). $C_{14}H_{16}N_2$ requires C, 79.2; H, 7.6; N, 13.2% m/e 212.131342. $C_{14}H_{16}$ requires 184.125194. $C_{12}H_{12}N_2$ requires 184.100043). 1H N.m.r., ^{13}C n.m.r. and mass spectra: see Appendix.

- b) Decomposition of 4,5,6,7-Tetrahydro-3-methyl-3-phenylindazole in Various Solvents. Small samples of the indazole (15-50 mg) were dissolved in a) DME (b.p. 85°), b) toluene (b.p. 111°) and c) p-xylene (b.p. 138°). The three solutions were heated under reflux in the dark under nitrogen while the reactions were monitored by t.l.c. and h.s.l.c. (both using alumina/methylene chloride). Solution a) was cooled after 6 days with a considerable quantity of reactant still remaining. No reactant was left in solution b) after 1 week and in solution c) after 1 day.

All three solutions were shown by the chromatographic methods to contain multiple products. None of these products could be identified.

- c) Acid Catalysed Isomerisation of 4,5,6,7-Tetrahydro-3-methyl-3-phenylindazole. The indazole (438 mg, 1.40 mmol) was dissolved in glacial acetic acid (30 ml) and the solution was kept at 95° in an atmosphere of nitrogen for 30 min. T.l.c. (alumina/methylene chloride, ether) showed that no reactant remained and that one main product had formed as well as a number of products with greater R_fs. The solution was neutralised with dilute sodium bicarbonate solution and the product was extracted with ether. After evaporation of the ether under reduced pressure, dry column chromatography

(alumina/methylene chloride) gave 4,5,6,7-tetrahydro-3-methyl-3a-phenylindazole (150 mg, 34%) as an orange oil which was shown to be pure by t.l.c. (Found: m/e 212.131706, 184.125175. $C_{14}H_{16}N_2$ requires 212.131342. $C_{14}H_{16}$ requires 184.125194.) 1H N.m.r., ^{13}C n.m.r. and mass spectra: see Appendix.

11. 2-(Di-p-tolylmethylene)cyclohexanone tosylhydrazone.⁴⁰

a) Decomposition in DME. The sodium salt of 2-(di-p-tolylmethylene)-cyclohexanone tosylhydrazone (3.39 g, 7.38 m mol) was heated under reflux in DME (75 ml) for 6 h. The usual work up, then dry column chromatography (alumina/methylene chloride), followed by cristallisation from a mixture of petrol (b.p. 60-80°) and ethanol gave 4,5,6,7-tetrahydro-3,3-di-p-tolylindazole (1.36 g, 61%) m.p. 102-103° (lit.,⁸¹ 101-102°). (Found: m/e 302.177541, 274.170931.

$C_{21}H_{22}N_2$ requires 302.178290. $C_{21}H_{22}$ requires 274.172142).

1H N.m.r., ^{13}C n.m.r. and mass spectra: see Appendix.

b) Decomposition of 4,5,6,7-Tetrahydro-3,3-di-p-tolylindazole in Toluene.

A solution of the indazole (811 mg, 2.68 m mol) in toluene (150 ml) was heated under reflux in the dark under nitrogen. T.l.c.

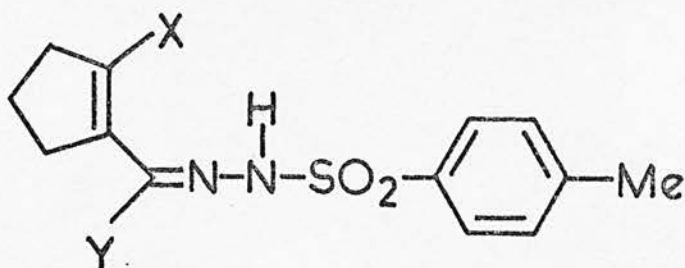
(alumina/benzene) showed that no reactant remained after 12 h. The solvent was then evaporated under reduced pressure to leave a white solid which was recrystallised from a mixture of petrol (b.p. 60-80°) and ethanol to give 4,5,6,7-tetrahydro-3,3a-di-p-tolylindazole (610 mg, 75%) m.p. 178-179°. (Found: C, 83.2; H, 7.4; N, 9.3.

m/e 302.176952, 274.172514. $C_{21}H_{22}N_2$ requires C, 83.4; H, 7.3;

N, 9.3%. m/e 302.178290. $C_{21}H_{22}$ requires 274.172142). 1H N.m.r.,

^{13}C n.m.r. and mass spectra: see Appendix.

APPENDIX 1.

Tosylhydrazonesa) ^1H n.m.r. spectral data (CDCl_3)*

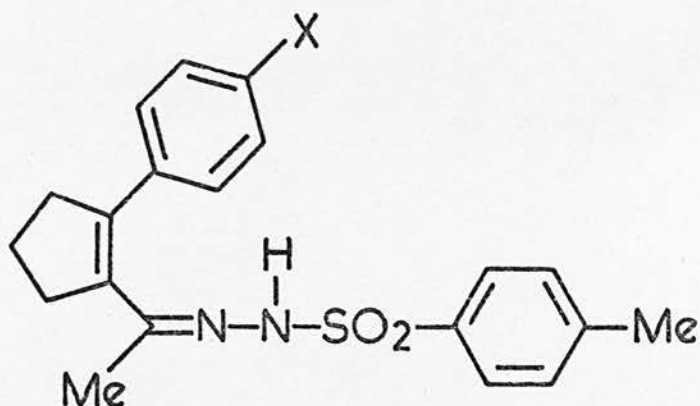
| X | Ph | CH_3 | Ph |
|---------------|--|------------------------------------|--|
| Y | Ph | CH_3 | H |
| Ar | 2.2-3.1 (m) | 2.03 (d, J 8Hz) 2.72 (d, J 8Hz) | 2.24 (d, J 8Hz) 2.7-3.0 (m) |
| CH_3 | 7.62 | 7.60, 8.08, 8.31 | 7.62 |
| CH_2 | 6.9 (m, 2H) 7.4 (m, 2H) 7.8 (m, 2H) | 7.4-7.7 (m, 4H) 8.1-8.4 (m, 2H) | 7.1-7.4 (m, 4H) 8.10 (quintet, J 7Hz, 2H) |
| -CH=N | | | 2.35 (s) |

b) I.r. spectral data (nujol): $\nu \text{ cm}^{-1}$

| | | | |
|----|------|------|------|
| NH | 3220 | 3210 | 3165 |
|----|------|------|------|

* In n.m.r. spectra, the multiplicity and the number of atoms responsible for the signal are not always quoted when they are obvious.

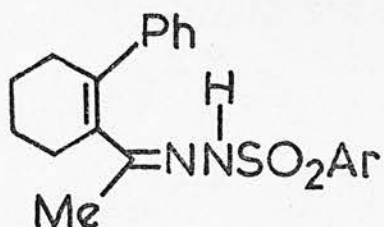
APPENDIX 1 (Continued)

a) $^1\text{H.N.m.r.}$ spectral data (CDCl_3)

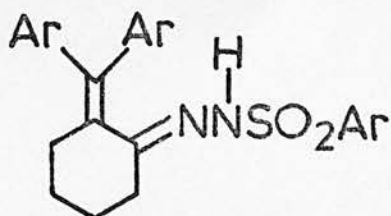
| X | H | CH_3 | F |
|--|---------------------------------|------------------|-----------------|
| Ar | 2.3-3.0 (m) | 2.1-3.2 (m) | 2.4-3.5 (m) |
| CH_3 | 7.58, 8.00 | 7.55, 7.71, 7.98 | 7.60, 7.97 |
| CH_2 | 7.2 (2H), 7.4 (2H), 7.9 (2H) | 6.9-8.5 (m, 6H) | 7.0-8.3 (m, 6H) |
| b) <u>I.r. spectral data (nujol): $\nu \text{ cm}^{-1}$</u> | | | |
| NH | 3165 | 3175 | 3175 |

APPENDIX 1 (Continued)

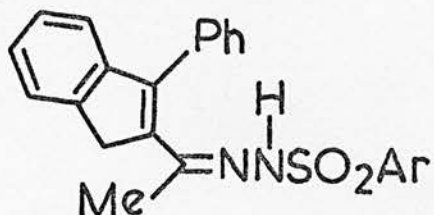
(1)



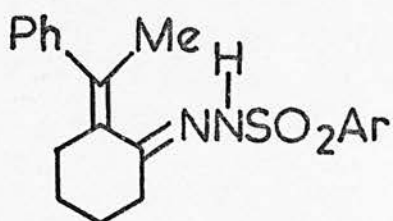
(3)



(2)



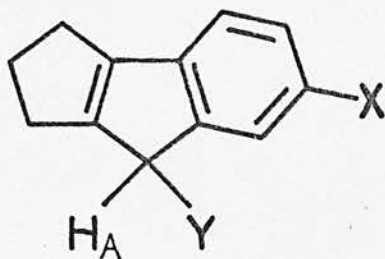
(4)

a) $^1\text{H N.m.r.}$ spectral data (CDCl_3)

Ar = p-tolyl

| Compound | (1) | (2) | (3) | (4) |
|--|------------------------------------|--------------|--|-------------|
| Ar | 2.1-3.1 (m) | 2.0-3.1 (m) | 2.14 (d, J 8Hz) 2.75 (d, J 8Hz) | 2.1-3.1 (m) |
| CH ₃ | 7.56, 8.72 | 7.61, 8.46 | 7.62, 8.24, 8.25 | 7.60, 8.24 |
| CH ₂ | 7.4-7.8 (m, 4H) 8.0-8.4 (m, 4H) | 6.22 (s, 2H) | 7.7 (m, 2H) 7.8 (m, 2H) 8.3 (m, 2H) | 7.3-8.6 (m) |
| b) <u>I.r. spectral data (nujol): ν cm⁻¹</u> | | | | |
| NH | 3195 | 3180 | 3220 | 3180 |

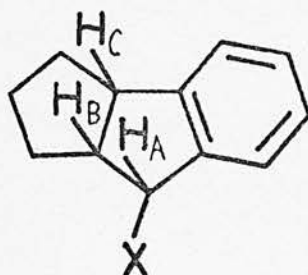
APPENDIX 3.

Indenesa) ^1H .m.r. spectral data

| X | H | H | CH_3 | F |
|----------------------------------|------------------|------------------|-------------------------|------------------|
| Y | Ph | CH_3 | CH_3 | CH_3 |
| Solvent | CCl_4 | CDCl_3 | CDCl_3 | CDCl_3 |
| Ar | 2.6-3.1 (m) | 2.6-3.0 (m) | 2.8-3.1 (m) | 2.8-3.3 (m) |
| CH_3 | | 8.74 (d, J 7Hz) | 7.68(s), 8.78(d, J 8Hz) | 8.77(d, J 7Hz) |
| CH_2 | 7.2-7.8 (m) | 7.3-7.8 (m) | 7.3-7.8 (m) | 7.3-7.8 (m) |
| H_A | 5.75 (bs) | 6.74(q, J 7Hz) | 6.82 (q, J 8Hz) | 6.80(q, J 7Hz) |
| <u>IR (cm$^{-1}$)</u> | | | | |
| | 232(52), | 170(47), 155(19) | 184(100), 169(32), | 188(83), 173(24) |
| | 204(100), | 142(100), | 156(68) | 160(100), |
| | 203(42), 202(33) | 141(35) | | 159(31) |
| | 191(19) | | | |

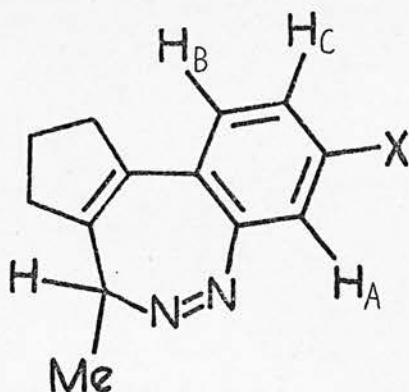
APPENDIX 4.

Indanes: ^1H .m.r. spectral data



| X | CH ₃ | Ph |
|-----------------|------------------------------|------------------------------|
| Solvent | CDCl ₃ | CCl ₄ |
| Ar | 2.7-3.0 (m) | 2.6-3.1 (m) |
| CH ₃ | 8.74 (d, J 7Hz) | |
| CH ₂ | 7.7-8.9 (m) | 7.7-9.1 (m) |
| H _A | 6.69 (quintet, J 7Hz) | 5.41 (d, J 9Hz) |
| H _B | 7.24 (quintet, J 8Hz) | 7.00 (quintet, J 8Hz) |
| H _C | 6.47 (t of d, J 8Hz, J' 4Hz) | 6.37 (t of d, J 8Hz, J' 4Hz) |

APPENDIX 5.

Diazepinesa) ^1H .m.r. spectral data (CDCl_3)

| X | H | CH_3 | F |
|---------------|-----------------|--------------------------------|-----------------|
| H_A | 2.26 (m) | 2.46 (d, J 1.5Hz) | |
| H_B | | 2.71 (d, J 8Hz) | |
| H_C | | 2.91 (d of d, J 8Hz, J' 1.5Hz) | |
| Ar | 2.5-2.8 (m, 3H) | | 2.4-3.1 (m) |
| CH_3 | 7.93 (d, J 6Hz) | 7.62 (s), 7.96 (d, J 6Hz) | 7.93 (d, J 6Hz) |
| aliphatics | 6.7-8.3 (m) | 6.7-8.4 (m) | 6.6-8.8 (m) |

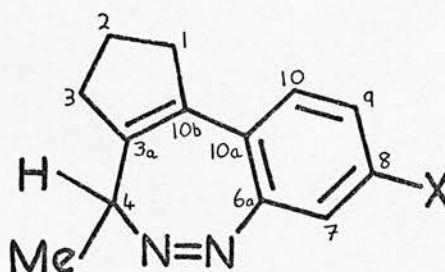
b) Mass spectral data

| | | |
|------------------|----------------------------|--------------------|
| 198(11), 170(63) | 212(14), 184(81), 169(32), | 216(10), 188(64), |
| 155(32), | 156(100) | 173(27), 160(100), |
| 142(100), | | 159(44) |
| 141(40) | | |

APPENDIX 5 (Continued)

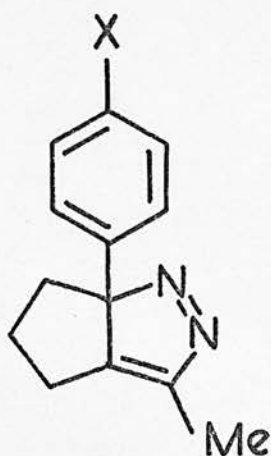
c) Ultraviolet spectral data (ethanol): nm

| H | CH ₃ | F |
|--|--|--|
| 210(ε 13300), 233(20200), 251(12400), 267(7900), 278(6400), 335(1200), 402(500) | 212(ε 13800), 234(23200), 252(14600), 268(8630), 279(6700), 338(1440), 410(480) | 209(ε 12400), 232(20600), 267(6400), 278(4200), 337(1700), 408(600). |

d) ¹³CN.m.r. spectral data (CDCl₃)

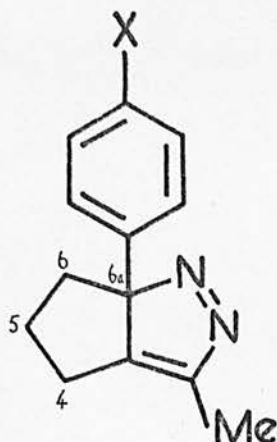
| X | Chemical shifts from T.M.S. (p.p.m.) |
|-----------------|---|
| H | CH ₃ : 16.7. C1-C3: 22.7, 32.6, 33.2. C4: 67.1. Aromatic and olefinic carbons: 125.5(d), 126.2(d), 127.6(d), 128.6(d), 136.1(s), 138.7(s), 150.6(s). |
| CH ₃ | 2 x CH ₃ : 16.7, 21.2. C1-C3: 22.7, 32.6, 33.0. C4: 67.0. Aromatic and olefinic carbons: 122.6(s), 125.8(d), 128.2(d), 128.9(d), 135.3(s), 135.9(s), 137.3(s), 150.3(s). |
| F | CH ₃ : 16.6. C1-C3: 22.6, 32.7, 33.1. C4: 67.6. C9: 113.6(J _{C-F} 22.2 Hz). C7: 116.1(J _{C-F} 22.6 Hz). C10a: 121.5. C10: 128.1(J _{C-F} 8.2 Hz). C3a, C10b: 135.5, 137.7. C6a: 151.0. C8: 159.1(J _{C-F} 247.8 Hz). |

APPENDIX 6

Cyclopenta[c]pyrazolesa) ^1H N.m.r. spectral data (CDCl_3)

| X | H | CH_3 | F |
|---|---|--------------------------------------|---------------------------------------|
| aromatics | 2.5–2.9 (m) | 2.6–3.0 (m) | 2.5–3.1 (m) |
| CH_3 | 7.69(s) | 7.64(s), 7.67(s) | 7.67(s) |
| aliphatics | 7.3–8.8 (m) | 7.2–8.8 (m) | 7.2–8.8 (m) |
| b) <u>Mass spectral data</u> | | | |
| | 198(2), 170(70), 155(28), 142(100) | 212(1), 184(60) 169(32), 156(100) | 216(1), 188(66), 173(21), 160(100) |
| c) <u>Ultraviolet spectral data (ethanol): nm</u> | | | |
| | 219(ϵ 5000), 267(2440) | 223(ϵ 7000), 265(3000) | 213(ϵ 6060), 265(2830) |

APPENDIX 6 (Continued)

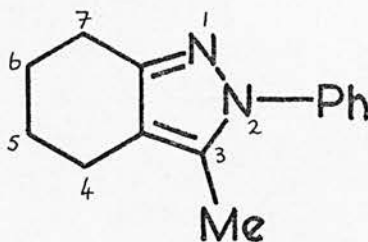
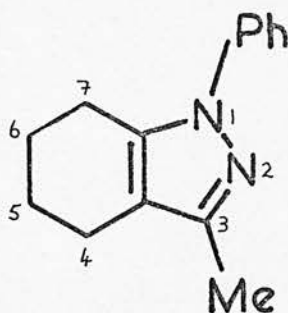


d) ^{13}C N.m.r. spectral data (CDCl_3)

| X | Chemical shifts from T.M.S. (p.p.m.) |
|---------------|---|
| H | CH_3 : 11.6. C4-C6: 19.5, 31.9, 33.9. C6a: 110.2. Aromatic carbons: 127.1(d,2C), 128.1(d,1C), 128.6(d,2C), 135.1(s,1C). Olefinic carbons: 148.5, 160.8 |
| CH_3 | 2 x CH_3 : 11.7, 21.0. C4-C6: 19.5, 31.9, 33.7. C6a: 109.8. Aromatic carbons: 126.8(d,2C), 129.2(d,2C), 131.8(s,1C), 137.5(s,1C). Olefinic carbons: 148.1, 160.7. |
| F | CH_3 : 11.7. C4-C6: 19.4, 31.8, 33.9. C6a: 109.3. Aromatic carbons: 115.4($J_{\text{C-F}}$ 21.5Hz,2C), 128.7($J_{\text{C-F}}$ 8.0Hz,2C), 130.6($J_{\text{C-F}}$ 2.8Hz,1C), 162.2($J_{\text{C-F}}$ 245Hz,1C). Olefinic carbons: 148.5, 160.3. |

APPENDIX 7.

Mixture of 4,5,6,7-Tetrahydro-3-methyl-1-phenylindazole and
4,5,6,7-Tetrahydro-3-methyl-2-phenylindazole



a) ^1H .m.r. spectral data

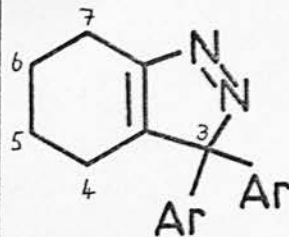
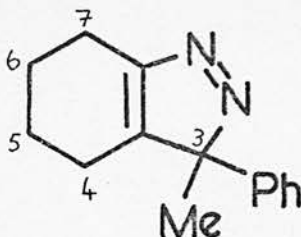
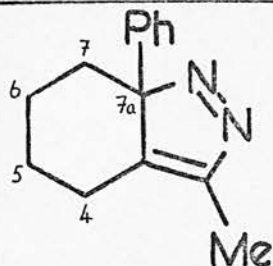
| CDCl_3 | C_6D_6 |
|--|---|
| 2.5–2.8 (m, 5H), 7.1–8.4 (m, 8H), 7.8 (s, CH_3) | 2.3–3.1 (m, 5H), 7.2–8.7 (m, 8H), 7.78(s, 0.75 CH_3), 8.12(s, 0.25 CH_3) |

b) ^{13}C .m.r. spectral data (CDCl_3): p.p.m.

CH_3 : 10.7 (34), 11.7 (86). Aliphatic carbons: 20.3 (176), 20.5 (78),
 22.7 (188), 23.0 (199), 23.5 (204), 23.8 (175). Aromatic and olefinic
 carbons: 115.4(s, 18), 116.2(s, 49), 122.5(d, 103), 124.3(d, 43), 125.9
 (d, 65), 126.7(d, 30), 128.9(d, 149), 134.3(s, 10), 138.4(s, 37), 140.2(s, 26)
 146.9(s, 51), 149.6(s, 17)

APPENDIX 8.

Tetrahydro-3H-indazoles



Ar = p-tolyl

a) ^1H .m.r. spectral data (CDCl_3)

2.73(s, 5H), 7.54(s, CH_3),
6.7-9.4(m, 8H)

2.6-3.1(m, 5H), 7.1-7.3(m, 2H),
7.7-8.5(m, 6H), 8.35(s, CH_3)

3.0(s, 8H), 7.0-8.4
(m, 8H), 7.68(s,
2 x CH_3)

b) Mass spectral data

212(18), 184(48),
169(48), 156(33),
155(44), 141(100)

212(16), 184(79), 169(73),
156(44), 155(79), 141(100)

302(8), 274(100),
259(31), 246(23),
245(50), 231(27)

c) ^{13}C .m.r. spectral data (CDCl_3)

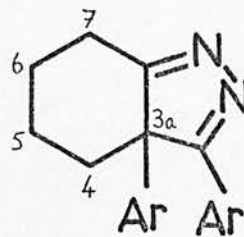
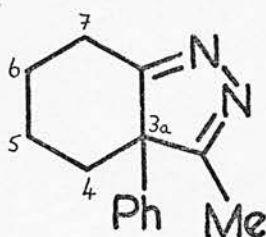
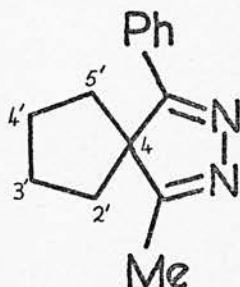
CH_3 : 11.1. C4-C7:
21.6, 24.8, 28.1, 37.2
C7a: 99.8. Aromatic
carbons: 127.4(d, 2C),
127.9(d, 1C), 128.8
(d, 2C), 134.1(s, 1C).
Olefinic carbons:
147.5, 150.7

CH_3 : 19.1. C4-C7: 21.7,
21.9, 22.3, 22.6. C3:
96.7. Aromatic carbons:
125.7(d, 2C), 127.8(d, 1C),
128.8(d, 2C), 135.4(s, 1C).
Olefinic carbons: 152.4,
152.9

2x CH_3 : 21.0.
C4-C7: 22.2, 22.4,
22.8, 23.3. C3:
104.1. Aromatic
carbons: 127.7(d),
129.3(d), 134.4(s),
137.6(s). Ole-
finic carbons:
150.9, 153.5

APPENDIX 9.

4H-Pyrazoles



Ar = p-tolyl

a) $^1\text{H N.m.r.}$ spectral data (CDCl_3)

2.0–2.3(m, 2H), 2.5–2.8
(m, 3H), 7.4–8.3(m, 8H),
7.73(s, CH_3)

2.6–3.2(m, 5H), 6.8–9.0
(m, 8H), 8.05(s, CH_3)

2.38(d, J 8Hz, 2H), 2.7–
3.2(m, 6H), 6.6–8.8(m, 8H),
7.69(s, 2x CH_3)

b) Mass spectral data

212(27), 184(34),
169(31), 156(29),
155(48), 142(47),
141(100)

212(26), 184(23),
170(23), 169(26),
143(62), 129(100)

302(48), 274(100),
157(96), 143(83)

c) $^{13}\text{C N.m.r.}$ spectral data (CDCl_3)

CH_3 : 13.1. C2'–C5':
27.8(2C), 33.5(2C).
C4: 67.9. Aromatic
carbons: 127.6(d, 2C),
128.7(d, 2C), 130.4
(d, 1C). C=N: 177.9,
181.1

CH_3 : 12.5. C4–C7:
21.3, 26.9, 29.3,
33.8. C3a: 63.3.
Aromatic carbons:
126.3(d, 2C), 128.0
(d, 1C), 129.6(d, 2C).
C=N: 180.2, 181.9

2x CH_3 and C4–C7: 21.0,
21.4, 21.5, 26.7(t),
29.6(t), 34.9(t). C3a:
67.6 Aromatic carbons:
126.5(d), 127.6(d),
129.2(d), 129.7(s),
130.2(d), 137.5(s),
140.7(s). C=N: 180,
182.9

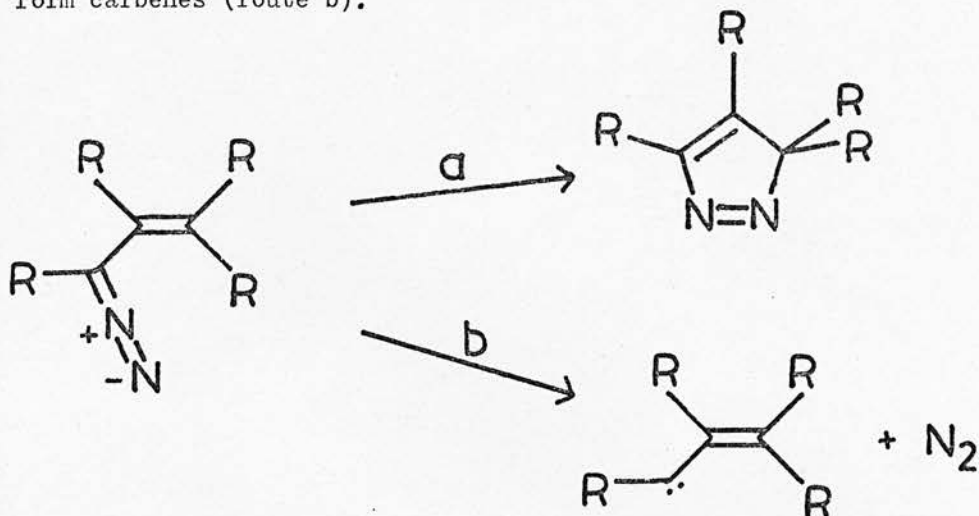
DISCUSSION

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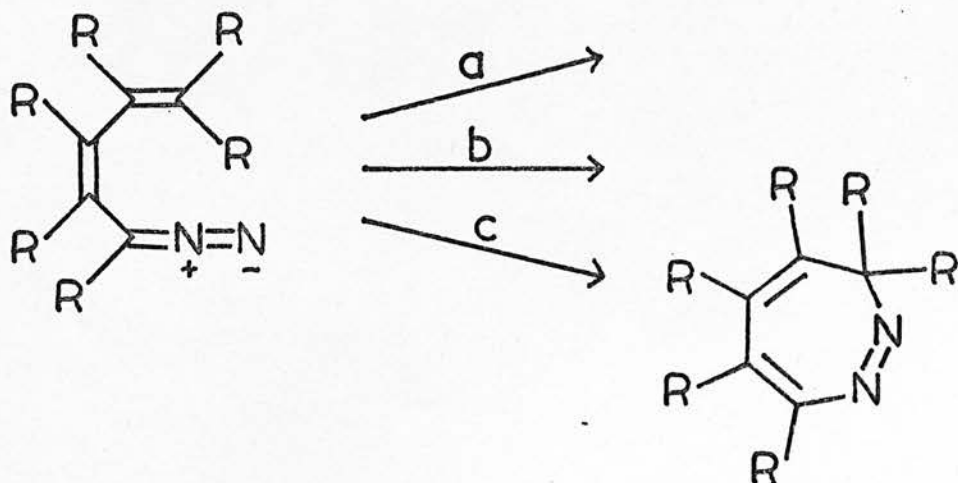
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PREAMBLE

It has been known for some years that the diazoalkenes produced by the base-induced decomposition of $\alpha\beta$ -unsaturated tosylhydrazones in aprotic solvents can cyclise to give pyrazoles (route a), and/or lose nitrogen to form carbenes (route b).



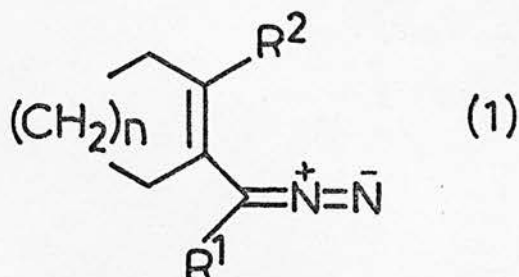
Sharp, Thorogood and Stanley^{40,43,44,81} were able to extend the unsaturated system to allow a third mode of reaction (route c). This was an 8π -electron ring closure to give a diazepine. These workers showed



that (a) was the preferred route if the $\alpha\beta$ -double bond of the tosylhydrazone was olefinic and the $\gamma\delta$ -double bond was aromatic, but the system could be

adapted to decompose via routes (b) or (c) if route (a) was inhibited in some way. They demonstrated that substituents on the diazoalkene determined the mode of decomposition, and in particular, that the nature and position of carbocyclic rings, with their geometrical constraints on the diazoalkene were of fundamental importance (see introduction).

The main object of this research was the study of diazoalkenes of type (1). By varying the ring size and the substituents R, it was hoped

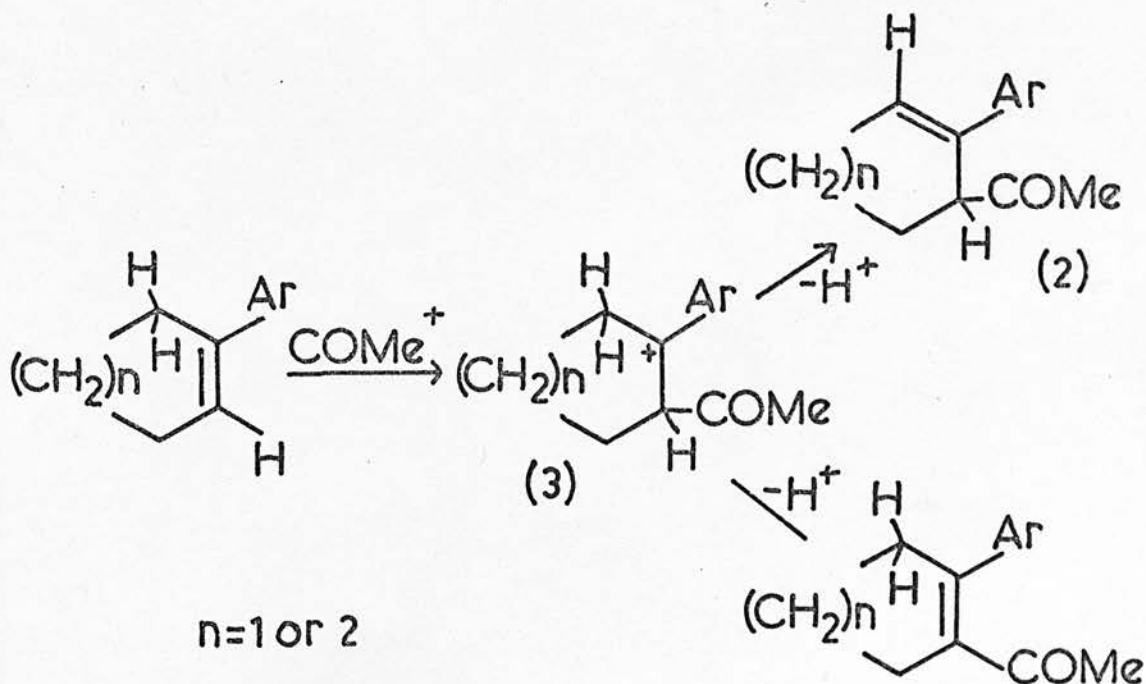


to gain a clearer understanding of the factors influencing the various possible modes of decomposition of diazoalkenes in aprotic solvents. In particular, it was hoped that with $R^2 = \text{aryl}$, 1,2-benzodiazepines could be synthesised in good yields by 1,7-ring closure, so extending the range of this synthesis of these rare compounds.⁸²

As the research progressed, it became useful to study related diazoalkenes, and a number of interesting reactions of the cyclisation products were also carried out.

SYNTHESIS OF $\alpha\beta$ -UNSATURATED CARBONYL COMPOUNDS
AND THEIR TOSYLHYDRAZONES

1. 1-Benzoyl-2-phenylcyclopentene was prepared along with 3-benzoyl-2-phenylcyclopentene by the base-catalysed cyclisation of 1,4-dibenzoyl-butane.⁶⁹ In the literature preparation,⁶⁹ the unwanted isomer was separated from the mixture by fractional crystallisation, but it was found more convenient to separate the isomers by dry column chromatography.
2. 1-Acetyl-2-arylcycloalkenes^{73,76,83} were prepared by the Friedel-Crafts acylation of 1-arylcycloalkenes. Mild conditions were used to ensure that no acylation of the aromatic rings took place. In all cases, the primary product was the $\beta\gamma$ -unsaturated ketone (2). This is in agreement with the work of Groves and Jones^{73,76,83} on the acylation



of 1-alkylcycloalkenes. Possible reasons for the formation of the non-conjugated isomer have been discussed by Groves and Jones⁷⁶, Groves⁸⁴ and Nenitzescu and Balaban.⁸⁵ The most likely explanation

appears to be that there is preferential elimination of a quasi-axial proton from the intermediate carbonium ion (3) and this is only possible from the γ -position. This argument is more substantial in the six-membered ring case than in the five.

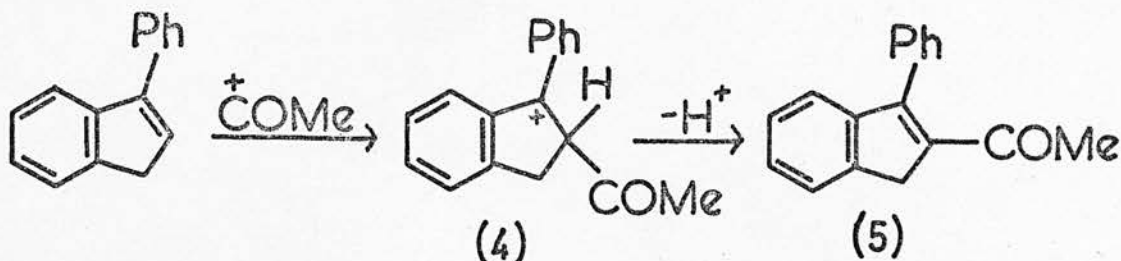
Whatever the precise explanation, it is clear that the transition state required to give the non-conjugated ketone is of lower energy than that required for the conjugated isomer. It must be said, however, that the conjugated isomer will have a certain loss of stability caused by steric interaction between the aryl and the acetyl groups, which are coplanar, and this will partially offset the gain in stability due to the conjugation. The relative stabilities of the two ketones were illustrated after the 3-acetyl-2-arylcycloalkene had come to equilibrium with its conjugated isomer in the presence of base. In no case was there a significant excess of the conjugated isomer, unlike the analogous 3-acetyl-2-alkylcycloalkenes ^{73,83} which at equilibrium can contain >90% of the conjugated isomer. In these cases, Groves and Jones⁸³ found that as the size of the alkyl group was increased, the equilibrium mixture of the ketones contained a greater proportion of the non-conjugated isomer.

In 1937, Allen and Rudoff⁸⁶ claimed that Friedel-Crafts acylation of 1-phenylcyclohexene gave 1-acetyl-2-phenylcyclohexene, but there is little doubt that their product was in fact 3-acetyl-2-phenylcyclohexene.

The separation of the two isomeric ketones proved to be a major task. At first, this was done by dry column chromatography (alumina/toluene), but this was very inefficient, and the later use of the Fischer Spaltrohr System distillation apparatus proved much more efficient and effective.

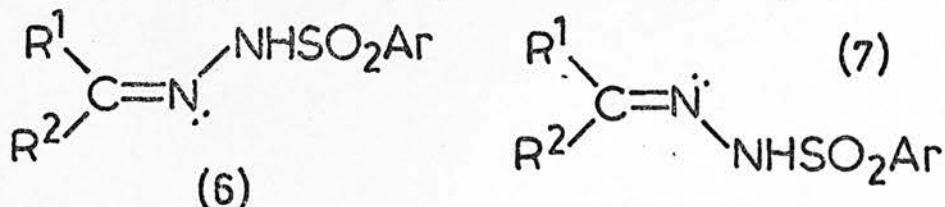
3. 2-Acetyl-3-phenylindene was prepared by the Friedel-Crafts acylation

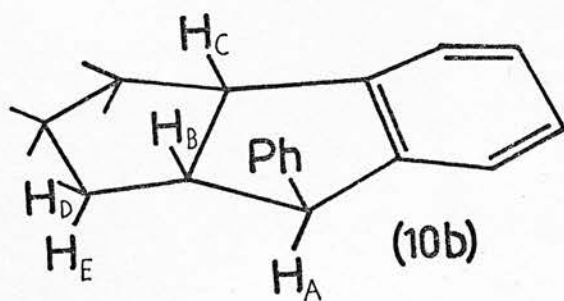
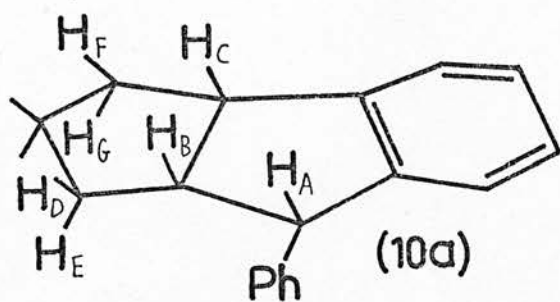
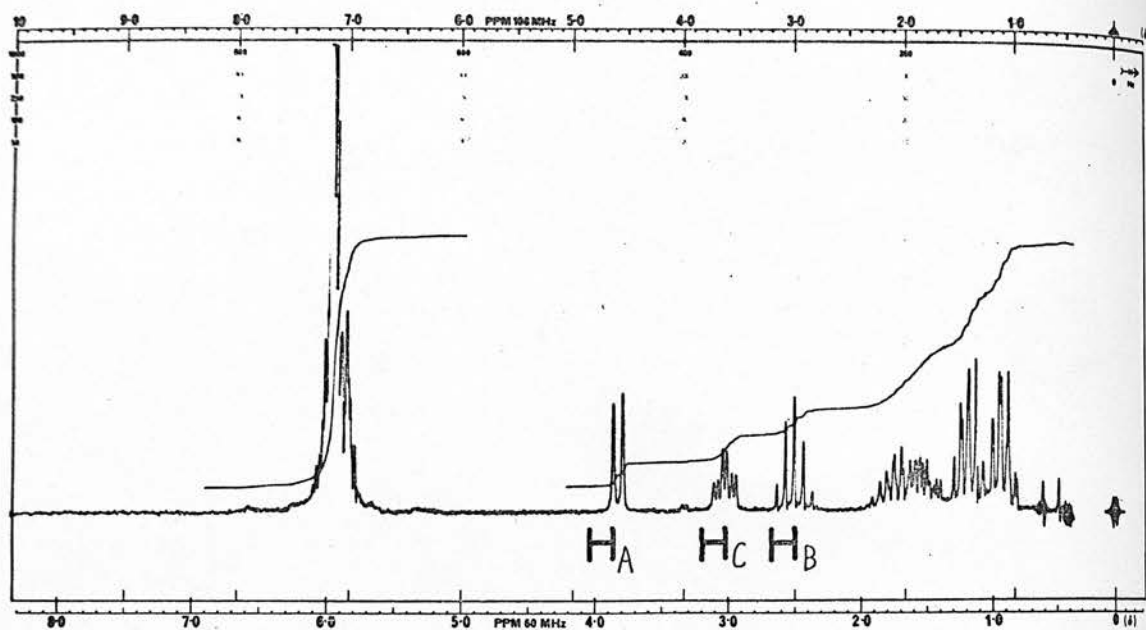
of 3-phenylindene. Unlike the acylation of 1-arylcycloalkenes, the aromatic ring in the indene ensures that the only proton which the carbonium ion (4) can eliminate is that which results in the formation of the conjugated ketone (5).



4. Other Carbonyl Compounds were prepared by relatively straightforward literature preparations.
5. Tosylhydrazones of $\alpha\beta$ -Unsaturated Carbonyl Compounds were prepared by condensation reactions, using as mild conditions as possible commensurate with the formation of product at a reasonable rate. The more heat that was used to drive a condensation to completion, the more side reactions became significant. The only non-routine tosylhydrazone preparation was that of 2-phenylcyclopenten-1-al tosylhydrazone which was prepared in ether because of its excessive solubility in alcoholic solvents.

All tosylhydrazones were identified by their i.r. and $^1\text{Hn.m.r.}$ spectra. The N-H stretch (ca. 3200cm^{-1}) often revealed two peaks, which could be attributed to the syn and anti isomers (6,7) both being present. This also resulted in a number of the melting points (with decomposition) of the tosylhydrazones not being very reproducible.

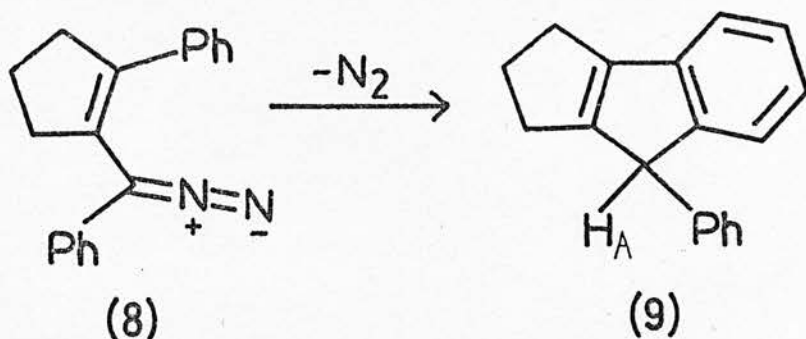




DECOMPOSITION OF THE SODIUM SALTS OF
THE TOSYLHYDRAZONES, AND RELATED REACTIONS

1. 1-Benzoyl-2-phenylcyclopentene tosylhydrazone.

The sodium salt of 1-benzoyl-2-phenylcyclopentene tosylhydrazone⁴³ was heated under reflux in cyclohexane. The reaction mixture became mauve after fifteen minutes, indicating the presence of the diazo-alkene (8). The colour slowly faded and a 95% yield of 1,2,3,4-tetrahydro-4-phenylcyclopenta [b]indene (9) was isolated. The identity of this compound was ascertained by spectroscopic and chemical evidence.



The ¹Hn.m.r. spectrum of the indene was not very informative except for a broad singlet at τ 5.75 which is the doubly benzylic proton H_A. The mass spectrum showed the molecular ion m/e232 which lost C₂H₄ to give the base peak m/e204.

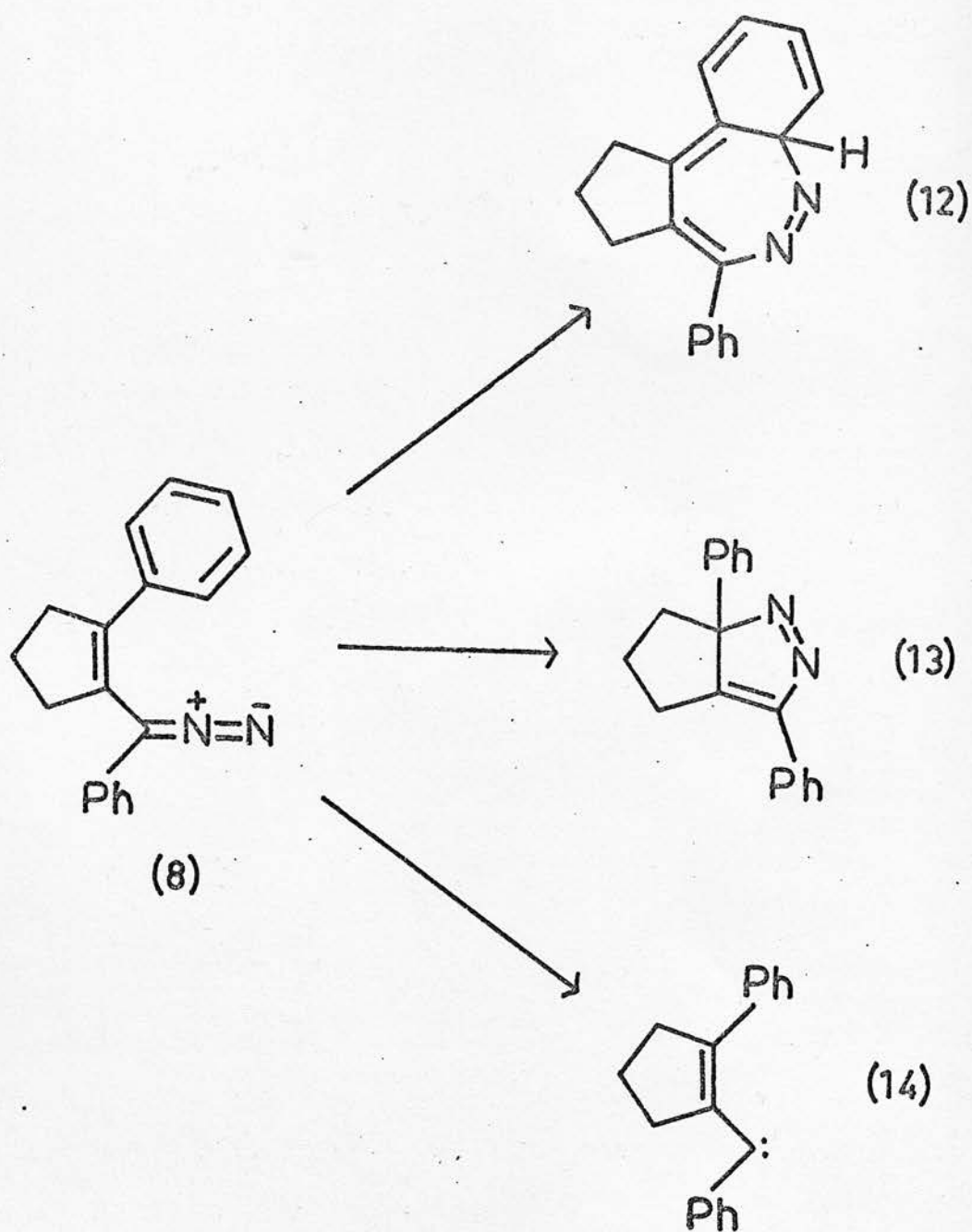
The identity of the indene was confirmed by its hydrogenation to 4-phenylcyclopenta[a]indane (10). This compound had a molecular ion m/e234, and a most interesting ¹Hn.m.r. spectrum which enabled the configuration and the conformation of the molecule to be determined. It is apparent, both from the mechanism of hydrogenation, and the structural constraints of two fused five-membered rings, that the incoming hydrogen atoms (H_B and H_C) in the hydrogenation must have a cis relationship to each other in the indane, thus two configurations are possible. H_A may be either cis (structure 10a) or trans (structure

10b) to H_B .

The doublet at $\tau 5.41$ cannot be other than H_A (J 9Hz). Irradiation at H_A collapsed the quintet at $\tau 7.00$ to a quartet, thus confirming H_B as the quintet. H_B therefore has virtually the same coupling constant (J 8-9Hz) to H_A , H_C , H_D , and H_E . Study of the Karplus curve^{87,88,89} for vicinal coupling constants indicates that the only way in which H_D and H_E can couple equally to H_B with J 8Hz is if the dihedral angles H_DH_B and H_EH_B are 20° and 140° (one must be 120° greater than the other). Construction of Drieding models indicated that such a conformation would make the dihedral angle H_AH_B either 20° (structure 10a) or 100° (structure 10b). The Karplus curve predicts that a dihedral angle of 100° gives a coupling constant of virtually zero, whereas 20° gives the desired constant of 8-9Hz. Thus, H_A , H_B , and H_C are all cis to one another.

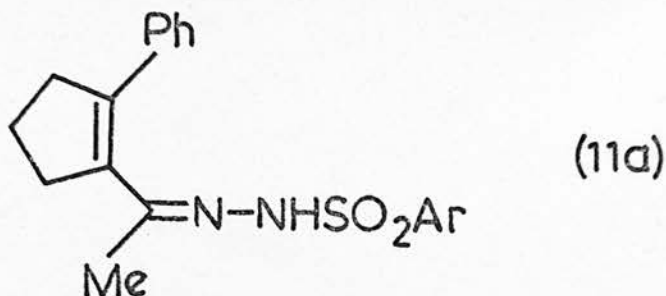
Simultaneous irradiation at H_A ($\tau 5.41$) and $\tau 6.37$ collapsed the quintet at H_B to a triplet, thus confirming H_C as the triplet (J 8Hz) of doublets (J 4Hz) at $\tau 6.37$. $J_{BC} = 8\text{Hz}$, hence the couplings from H_C to H_F and H_G must be 8Hz and 4Hz. The Drieding model showed the dihedral angles to be $H_CH_F = 5^\circ$ and $H_CH_G = 115^\circ$. The Karplus curve⁸⁷ predicts that the coupling constants will be J_{CF} 8-11Hz and J_{CG} 1-3Hz. These values are in reasonable agreement with the values found in the spectrum. It would seem likely that the reason for the specific attack of the hydrogen molecule on one side of the indene is due to the bulk of the phenyl group shielding the other face.

The reaction of the diazoalkene (8) will now be considered. The formation of a quantitative yield of indene (9) is at first rather surprising. Diazoalkenes with phenyl groups on the diazo-carbon are known to be more stable than their analogues with alkyl groups¹ and in acyclic systems Brewbaker and Hart¹³ have shown that a β -phenyl accel-



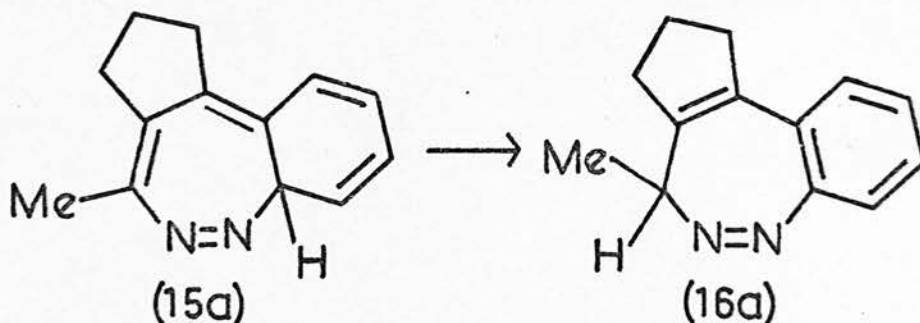
Scheme 1

erates the rate of cyclisation to 3H-pyrazoles. The red coloration seen in the decomposition (and not observed in the decomposition of 1-acetyl-2-phenylcyclopentene tosylhydrazone (11a)) indicates that the

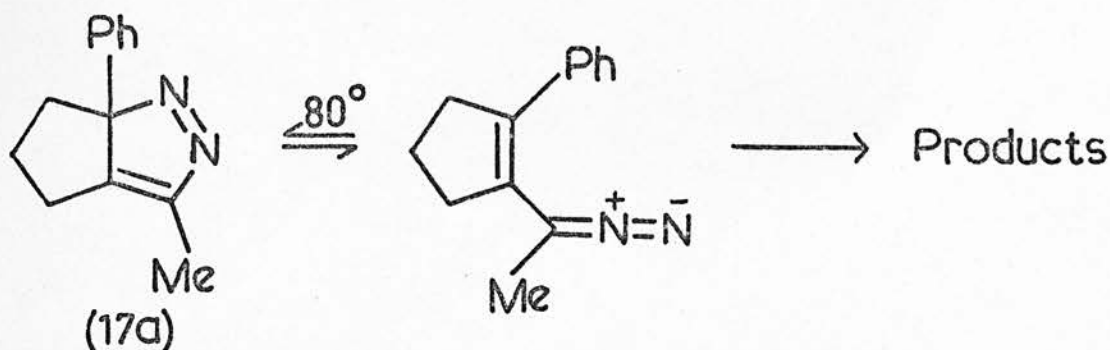


diazoalkene (8) is indeed relatively stable. This intermediate has three possible modes of decomposition (scheme 1).

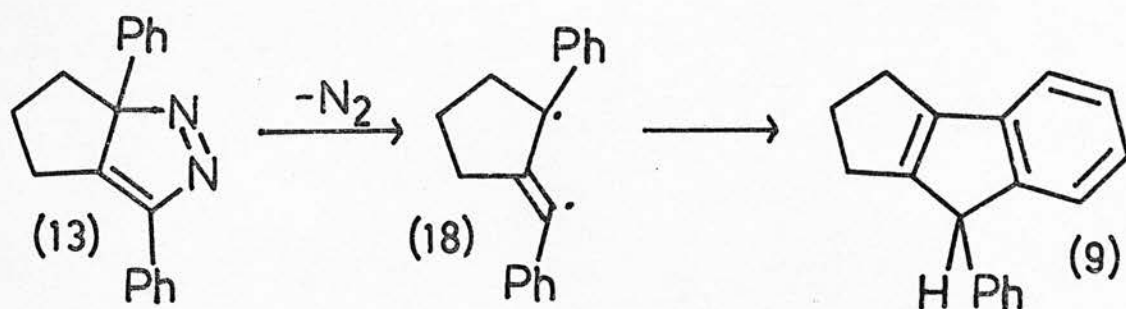
It would seem most unlikely that the indene (9) is formed via the diazepine (12), as the analogous compound (15a) readily rearranges via a 1,5 suprafacial hydrogen migration³³ to give the diazepine (16a) which is stable under reaction conditions (see later).



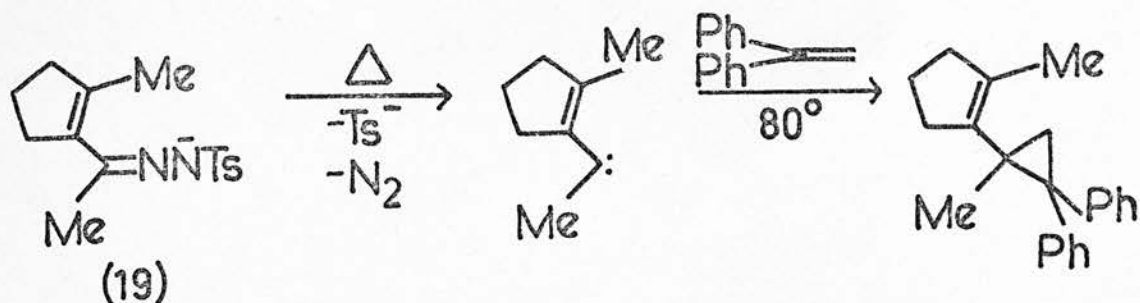
Formation of the indene (9) via the pyrazole (13) is possible, and it could happen in two ways. The pyrazole (13) could undergo the reverse reaction to the diazoalkene (8) which could then lose nitrogen to form the carbene (14). This is quite possible in the light of the decomposition of 4,5,6-trihydro-3-methyl-6a-phenylcyclopenta[c]pyrazole (17a), which is known to reverse to the diazoalkene (see later).



The other route by which pyrazole (13) could form the indene is via the diradical species (18) formed by two-bond cleavage of (13).

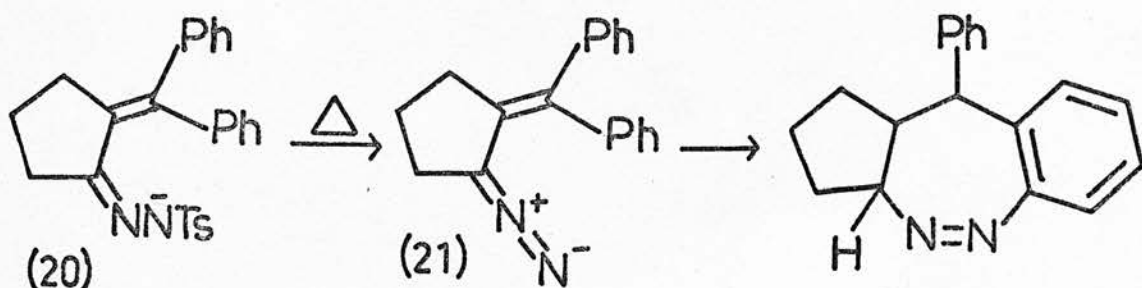


The most likely route for the formation of indene (9) is via the direct loss of nitrogen from the diazoalkene (8) to give the carbene (14). Such a carbene would be thermally generated as a singlet, but by analogy with diphenylcarbene, might have a triplet ground state. An attempt was made to trap any carbene formed in the decomposition of diazoalkene (8), by carrying out the tosylhydrazone decomposition in the presence of 1,1-diphenylethylene. This olefin is known to be a carbene trap which is particularly effective for triplets.⁹⁰ Indeed, it has been shown⁹¹ that 1,1-diphenylethylene traps diphenylcarbene >100 times more rapidly than do non-conjugated olefins. However, no adduct was found in the reaction, the indene being formed as in the absence of trap. Under analogous conditions, 1-methyl-2-acetylcyclopentene tosylhydrazone (19) gave a good yield of adduct. Thus, in the decomposition of 1-benzoyl-2-phenylcyclopentene tosylhydrazone, if

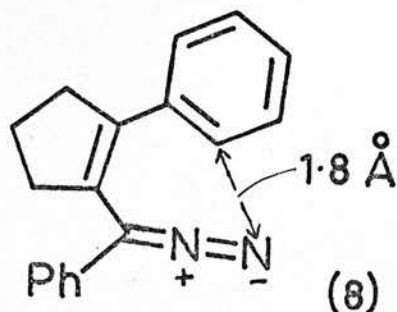
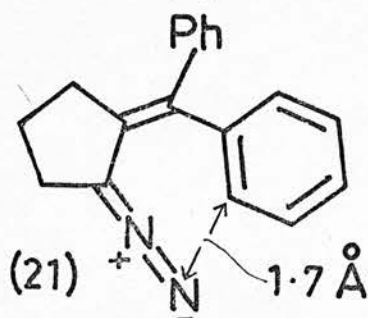


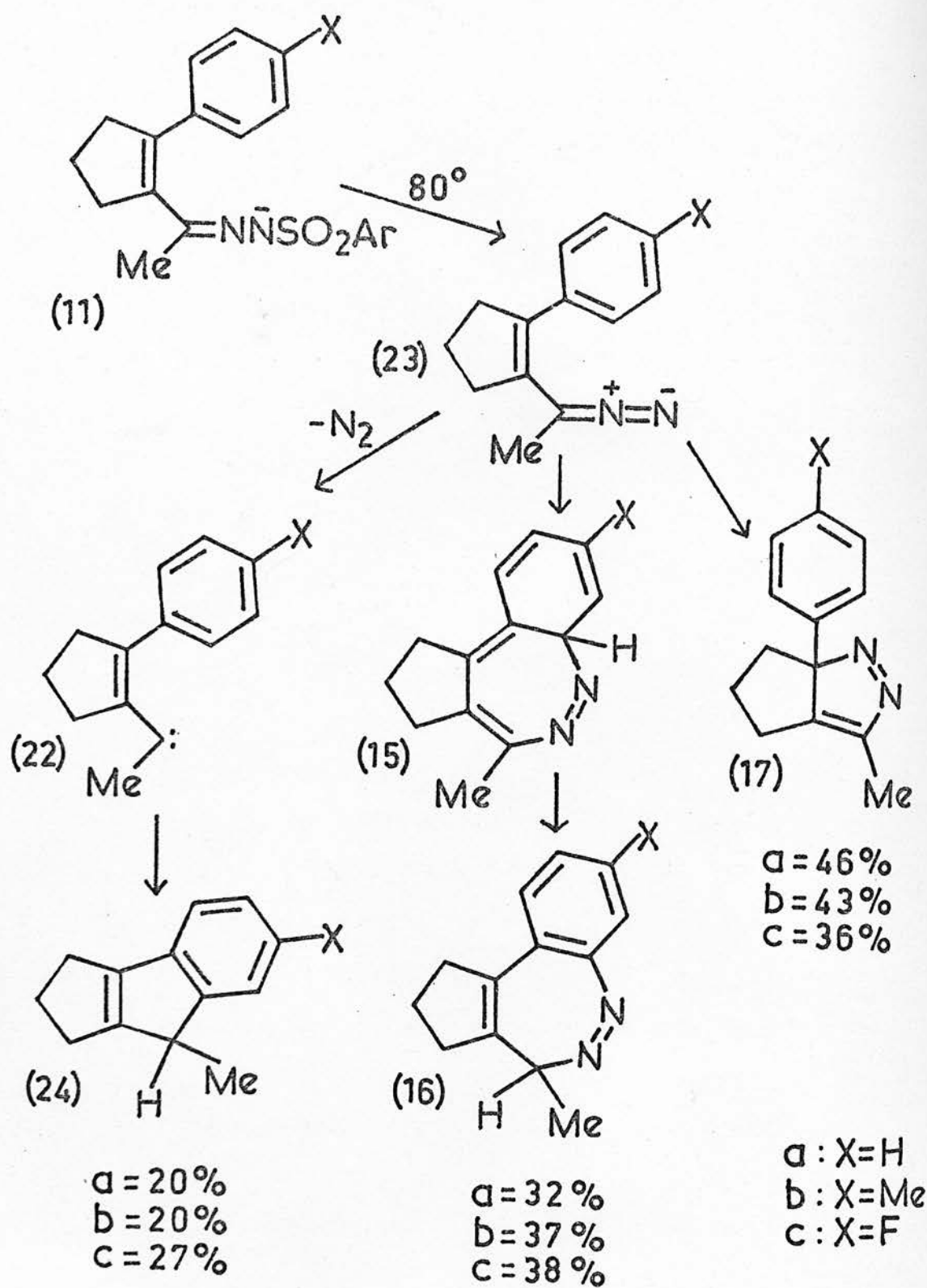
the carbene is formed, it inserts very quickly, probably as a singlet.

It is of interest to compare this decomposition with the superficially analogous decomposition of 2-diphenylmethylenecyclopentanone tosylhydrazone (20)⁴⁰ which gave no hydrocarbon, and an 80% yield of diazepine. The probable reason for the difference in behaviour is



due to a better overlap of the diazo group over the aryl in diazoalkene (21) than in (8). Drieding models illustrate that the interaction of the two phenyl groups in (21) favours a molecular geometry which is suitable for diazepine formation. Furthermore, the distance between the two ends of the 8π -electron system which must undergo a conrotatory ring closure to form the diazepine is ca 0.1 Å less in the case of diazoalkene (21) than for diazoalkene (8).





Scheme 2

A contributing factor in the formation of the indene (9) may be that the carbene (14) is stabilized by delocalisation both in the phenyl group on the diazo-carbon of the diazoalkene (8) and also through the double bond into the other phenyl group. This may lower the energy of the transition state between the diazoalkene and the carbene.

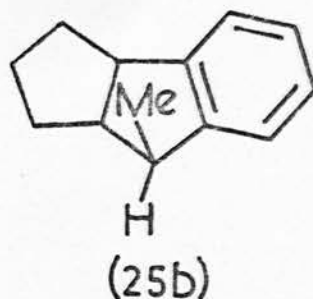
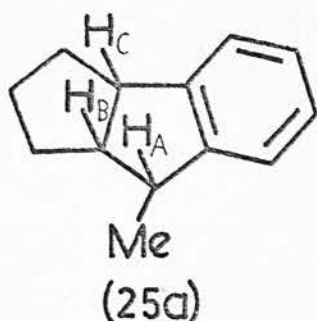
2. 1-Acetyl-2-arylcyclopentene tosylhydrazones.

The sodium salts of the 1-acetyl-2-arylcyclopentene tosylhydrazones (11, scheme 2) were heated under reflux in DME. No red colour, which would have indicated the presence of the diazoalkene (23) was observed in the decompositions of salts (11a) and (11b), but a slight red colour developed in the decomposition of the fluorocompound (11c). All these reactions eventually became yellow coloured and the standard work-up followed by separation of the compounds by column chromatography afforded 1,2,3,4-tetrahydro-4-methylcyclopenta[b]indenes (24), 1,2,3,4-tetrahydro-4-methylbenzo[c]cyclopenta[e]-[1,2]-diazepines (16) and 6a-aryl-4,5,6-trihydro-3-methylcyclopenta[c]pyrazoles (17).

The identity of the indenenes (24) was established by spectroscopy and also by the hydrogenation of indene (24a) to the indane. The mass spectra of the indenenes gave a large molecular ion which readily lost C_2H_4 from the cyclopentene ring. This cracking pattern is in agreement with that of 1,2,3,4-tetrahydro-4-phenylcyclopenta[b]indene (9). The 1H n.m.r. spectra of the indenenes (24) showed a benzylic proton (τ 6.8,q,J 7Hz) split by the methyl group (τ 8.8,d).

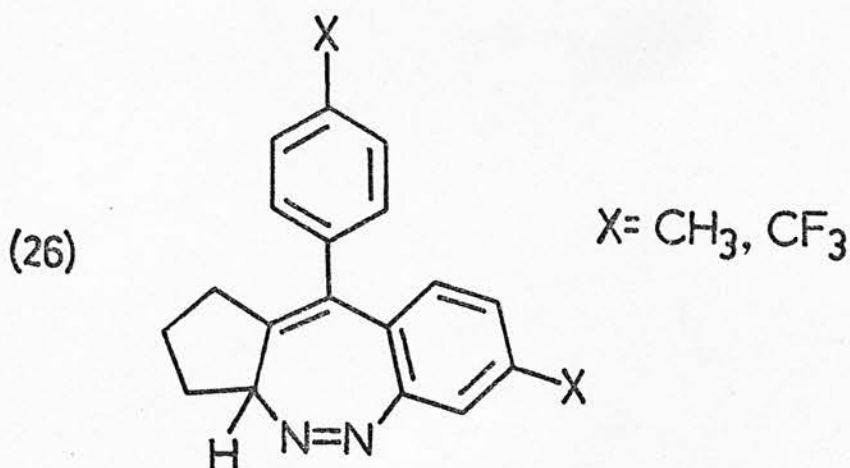
The indene (24a) was hydrogenated under a pressure of four atmospheres. Examination of the product by g.l.c. (1% SE 30) indicated the formation of two products in the ratio 8 to 1. G.l.c.-m.s. showed that both compounds had molecular ions m/e 172, and the compounds had almost identical cracking patterns, indicating their isomeric nature.

The products were apparently the two isomers of 4-methylcyclopenta-[a]indane (25a) and 25b).



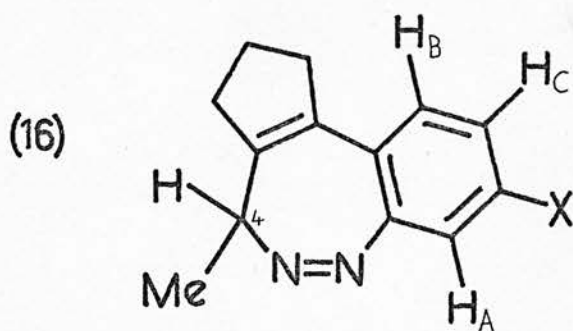
The great excess of one isomer resulted in the ^1H .n.m.r. spectrum apparently showing only one compound. This was readily identified as (25a) by reasoning similar to that used to identify 4-phenylcyclopenta[a]indane (10a). The quintet of H_B (τ 7.24, J 8Hz) proves that H_A , H_B and H_C are all cis to each other.⁸⁷ The more deshielded quintet (τ 6.69) must be H_A because of the proximity of the aromatic ring. It is likely that the smaller methyl group in (24a) compared to the phenyl group in the analogous indene (9) means that there is a smaller steric effect inhibiting an incoming hydrogen molecule from attacking the double bond on the same side of the molecule as the substituent. Hence hydrogenation of indene (24a) gives a small amount of indane (25b) whereas hydrogenation of (9) gives no (10b).

The benzodiazepines (16) were identified by their mass, ultraviolet and n.m.r. spectra. All three diazepines gave mass spectra with small peaks due to the molecular ions which readily eliminated nitrogen (the M^+-28 peak was shown to be due to loss of N_2 and not C_2H_4 by exact mass determination). Further fragmentation resulted in loss of $\cdot\text{CH}_3$ and C_2H_4 (base peak) from the M^+-28 ion, the cracking pattern being confirmed by metastable peaks. The ultraviolet spectra of the benzodiazepines (16) showed excellent agreement both in terms of wavelength and extinction coefficients with the spectra of benzodiazepine (26).⁴⁰

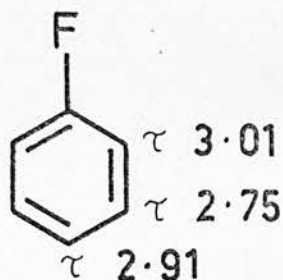


The $^1\text{Hn.m.r.}$ spectra of the diazepines (16) revealed certain interesting differences between the compounds caused by their different substituents. In (16a) and (16b) the azo group deshields H_A in addition to the deshielding effect of the aromatic ring. The de-

a: $X = \text{H}$
 b: $X = \text{Me}$
 c: $X = \text{F}$



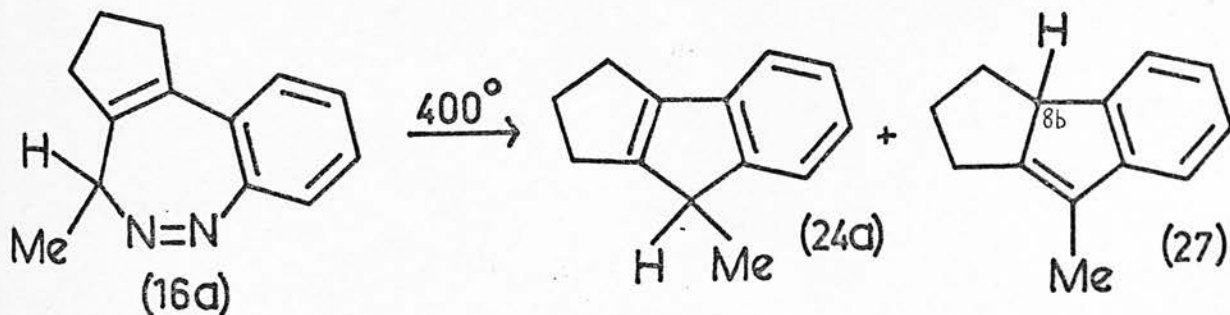
shielding effect of azo groups is well known.^{44,92} In (16c), however, the fluorine apparently shields its ortho protons to the extent that H_A did not absorb at significantly lower field than the other aromatic protons. This is in agreement with the $^1\text{Hn.m.r.}$ spectrum of fluoro-benzene in which the ortho protons are shielded.⁹³ In (16b) the methyl substituent enables the ortho and meta coupling to be seen



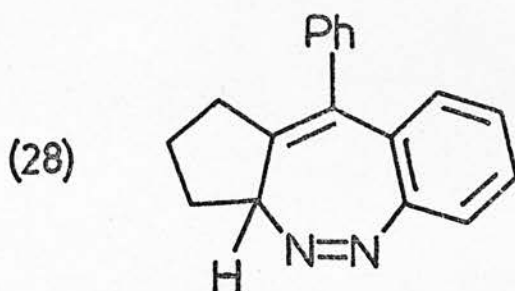
(J_{BC} 8Hz, J_{AC} 1.5Hz). Irradiation on part of the aliphatic multiplet (τ 7.5) in (16a) collapsed the methyl doublet (τ 7.93) to a singlet.

The identity of the diazepines was confirmed by their $^{13}\text{C}_{n.m.r.}$ spectra. The proton decoupled spectra showed C-4 to absorb at 67 p.p.m. in good agreement with the chemical shifts of analogous carbon atoms in other benzodiazepines.⁸¹ In (16c) the fluorine couples with the aromatic ring carbons with almost identical coupling constants to those found in fluorobenzene.⁹⁴

1,2,3,4-Tetrahydro-4-methylbenzo[c]cyclopenta[e]-[1,2]-diazepine (16a) was pyrolysed in a vacuum furnace at 400°. The product was collected in a cold trap and was shown by g.l.c. and g.l.c.-m.s. to contain two isomeric compounds (ratio 2:1) which were identified as 1,2,3,4-tetrahydro-4-methylcyclopenta[b]indene (24a) and 1,2,3,8b-tetrahydro-4-methylcyclopenta[a]indene (27) respectively. This is an analogous reaction to the thermolysis of benzodiazepine (28) which

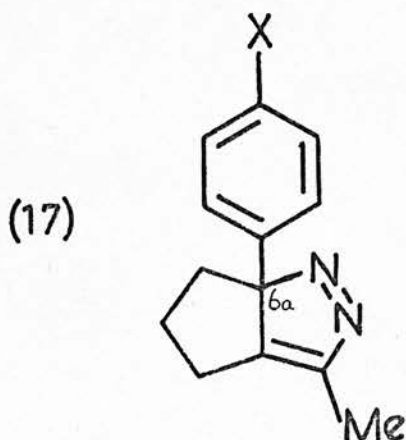


gave isomeric indenenes.⁹⁵ The thermolysis products of (16a) could not



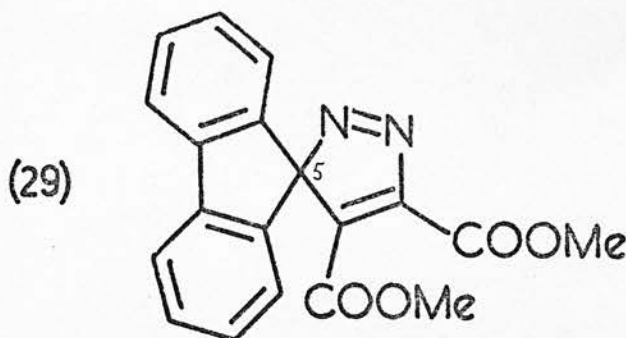
be separated, but comparison with an authentic sample of (24a) by g.l.c.-m.s. and $^1\text{Hn.m.r.}$ spectroscopy identified the major component in the mixture as (24a). The isomeric compound was identified as (27) by its $^1\text{Hn.m.r.}$ spectrum which showed H-8b as part of a multiplet ($\tau 6.3-7.0$) and had a low field methyl singlet ($\tau 8.00$).

The 3H-pyrazole (17) was identified by its mass and n.m.r. spectra. The mass spectra were almost identical to the spectra of the corresponding benzodiazepines (16), a fact which is to be expected as the fragmentation of both sets of compounds is governed by the facile elimination of nitrogen, followed by loss of C_2H_4 from the five-membered ring. The $^1\text{Hn.m.r.}$ spectra of the 3H-pyrazoles (17) revealed very little; only methyl singlets and aliphatic and aromatic multiplets. The $^{13}\text{Cn.m.r.}$ spectra, by comparison, were most informative. C-6a absorbed at 110 p.p.m. which is in excellent agreement with the corresponding carbon (C-5) in the spiropyrazole (29) which absorbs at



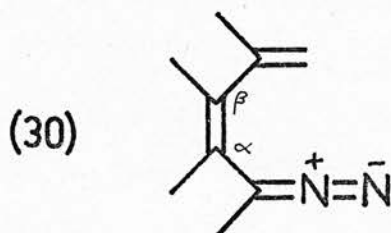
a: X=H
b: X=Me
c: X=F

109.8 p.p.m.⁹⁶ (cf. the sp^3 carbon in the diazepine (16) which absorbed at 67 p.p.m.).



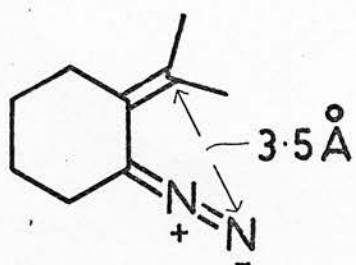
The olefinic carbons in (17) absorbed downfield of the aromatics, at 148 and 161 p.p.m. All the carbons in the $3H$ -pyrazoles (17) were accounted for in the spectra, and the fluorine-carbon coupling constants in (17c) all agreed closely with those in fluorobenzene.⁹⁴

The mechanism of the decomposition of 1-acetyl-2-arylcyclopentene tosylhydrazones in aprotic solvent is clearly of great importance in the understanding of the decompositions of similar cyclic tosylhydrazones, as it results in the formation of all three types of product found in such decompositions,^{40,43} i.e. pyrazoles, diazepines and unsaturated hydrocarbons. As was mentioned in the introduction to this Thesis, diazoalkenes (30) in which carbocyclic rings join either the diazo-carbon and $C\alpha$, or $C\alpha$ and $C\beta$, cyclise to initially give

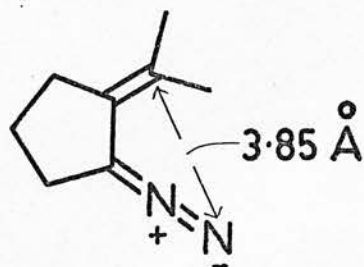


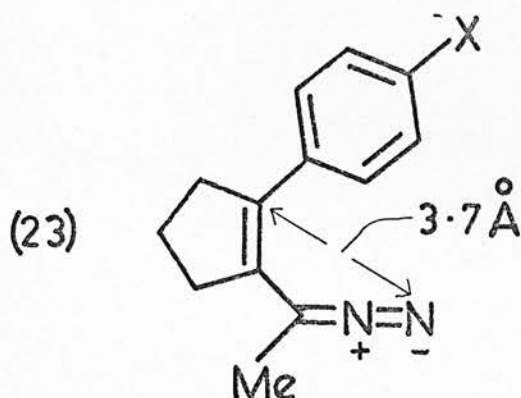
$3H$ -pyrazoles if this mode of reaction is possible, given the geometrical constraints on the molecule. Such a cyclisation is a 6π -electron disrotatory ring closure which requires the π -system to be approx-

(31)

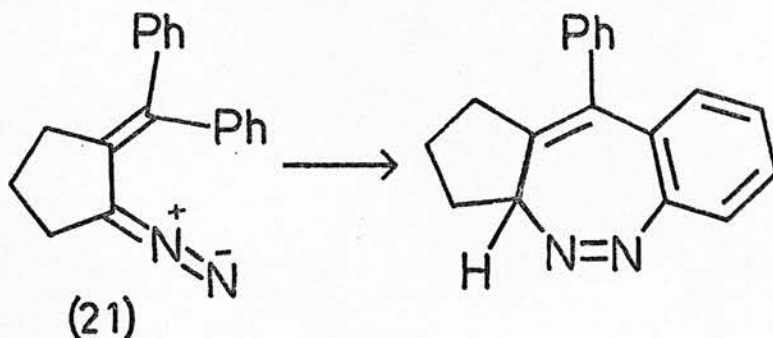


(32)



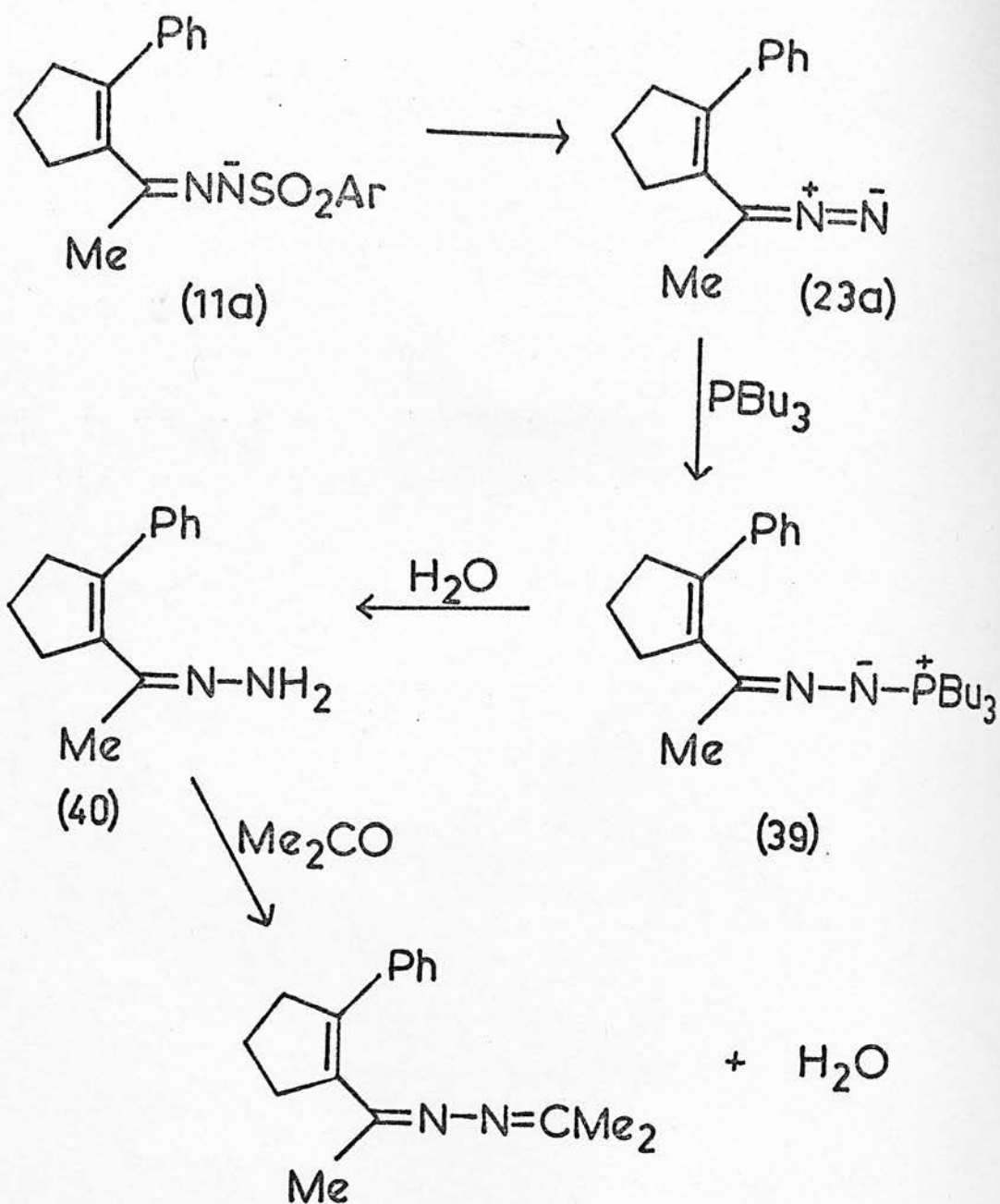


The next problem which the mechanism must explain is why both the diazepine (16) and the indene (24) are formed in addition to the pyrazole (17). As was mentioned in the discussion of the decomposition of 2-diazobenzyl-1-phenylcyclopentene (8), diazoalkene (21) has a



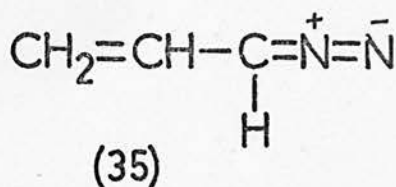
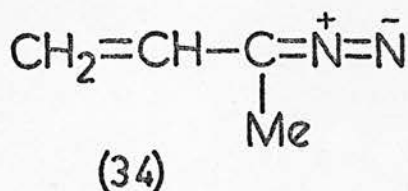
geometry more suitable for cyclisation to a diazepine than have diazoalkenes (8) and (23). However, diazoalkene (8) is more stable than (23a) due to the phenyl group on the diazo-carbon¹ in (8). This fact is supported by the red coloration in the decomposition of 1-benzoyl-2-phenylcyclopentene tosylhydrazone, and its absence in the decomposition of 1-acetyl-2-phenylcyclopentene tosylhydrazone. It appears that the higher ground state energy of diazoalkene (23) compared to (8) enables it to surmount energy barriers to form diazepine (16) and pyrazole (17) even though its molecular geometry is such that a diazoalkene with the same geometry around the α -system (8), but greater stability, is unable to surmount such barriers.

A similar explanation was given by Brewbaker and Hart¹³ to explain



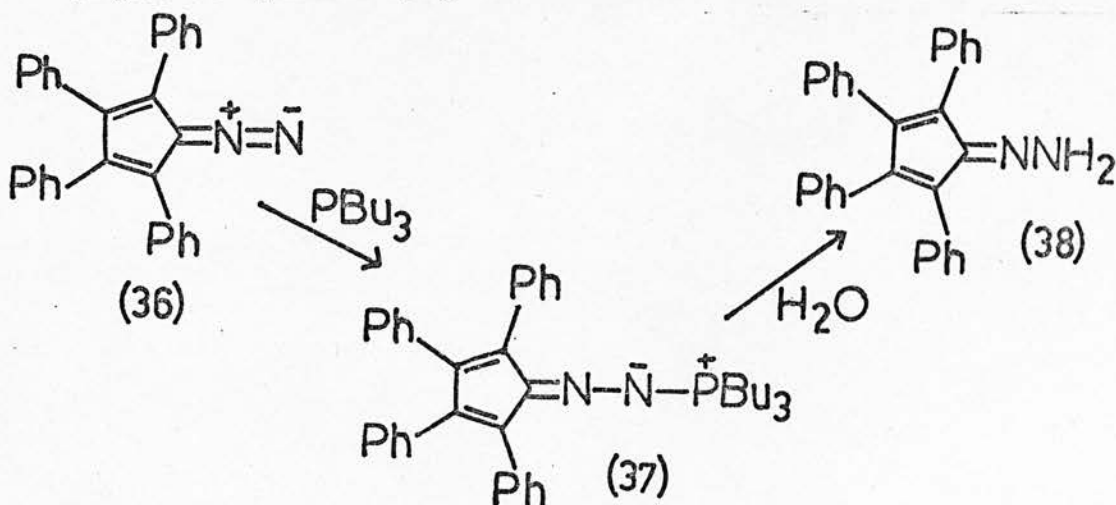
Scheme 3

why 3-diazobut-1-ene (34) cyclises to give a pyrazole thirteen times faster than 3-diazopropene (35). It is well known¹ that methyl groups

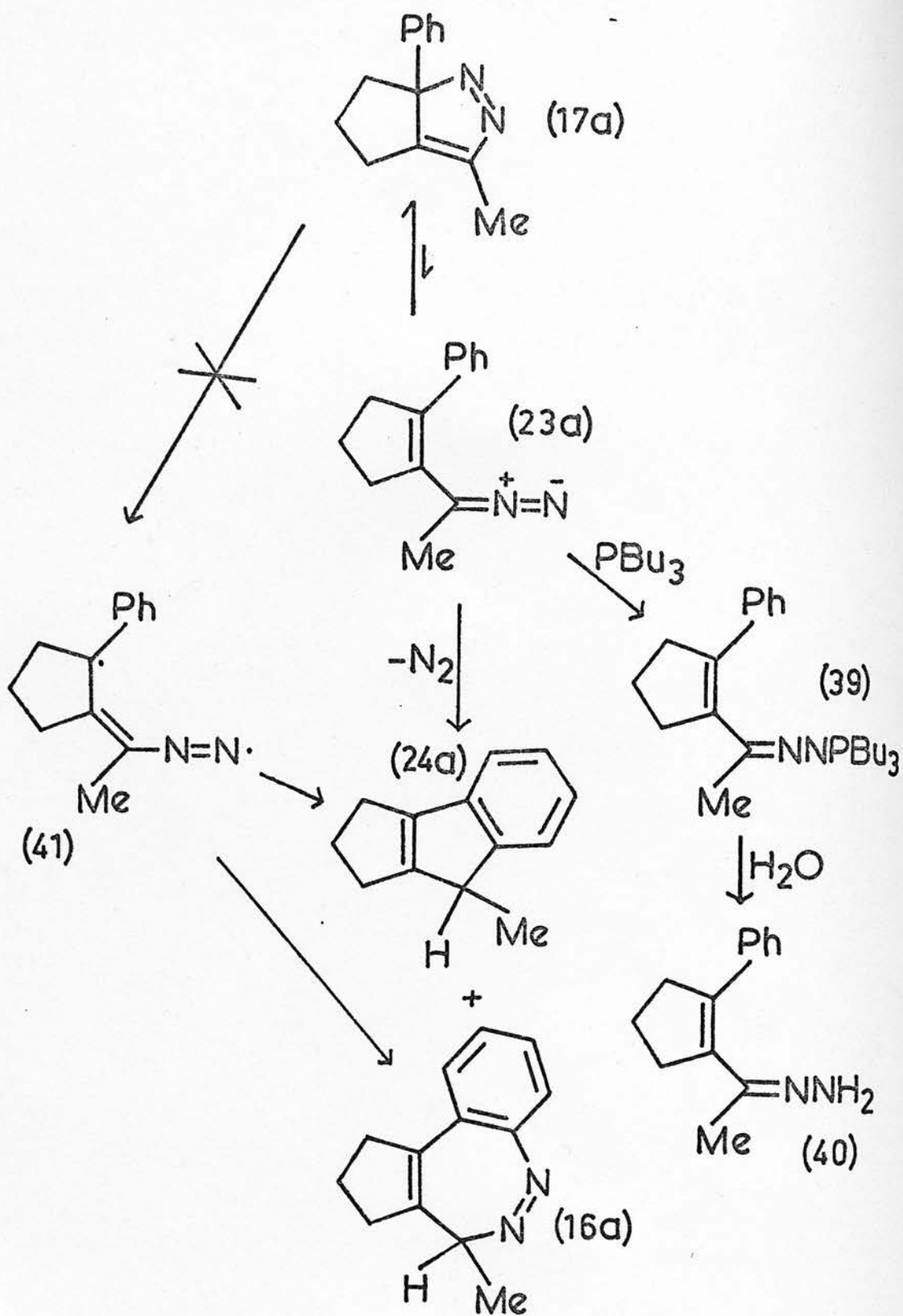


on the diazo-carbon destabilize diazoalkenes relative to the unsubstituted compound, just as corresponding aryl groups stabilize them.

The intermediacy of the diazoalkene (23) in the decomposition of 1-acetyl-2-arylcyclopentene tosylhydrazone (11) was verified by the adduct which was formed when the salt was decomposed in the presence of tri-*n*-butylphosphine. It has been known for many years⁹⁷ that diazoalkanes add to phosphines to give phosphazines, and it has recently been shown⁹⁸ that the adduct (37) of diazotetraphenylcyclopentadiene (36) with tri-*n*-butylphosphine readily hydrolyses during the work-up to give the hydrazone (38).



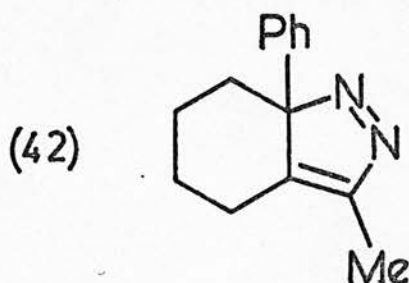
Likewise, the phosphazine (39) formed from 1-(1-diazoethyl)-2-phenylcyclopentene (23a) and tri-*n*-butylphosphine hydrolysed during the work-up to form 1-acetyl-2-phenylcyclopentene hydrazone (40) which was identified by ¹Hn.m.r. and i.r. spectroscopy, and by its condensation with acetone (scheme 3).



Scheme 4

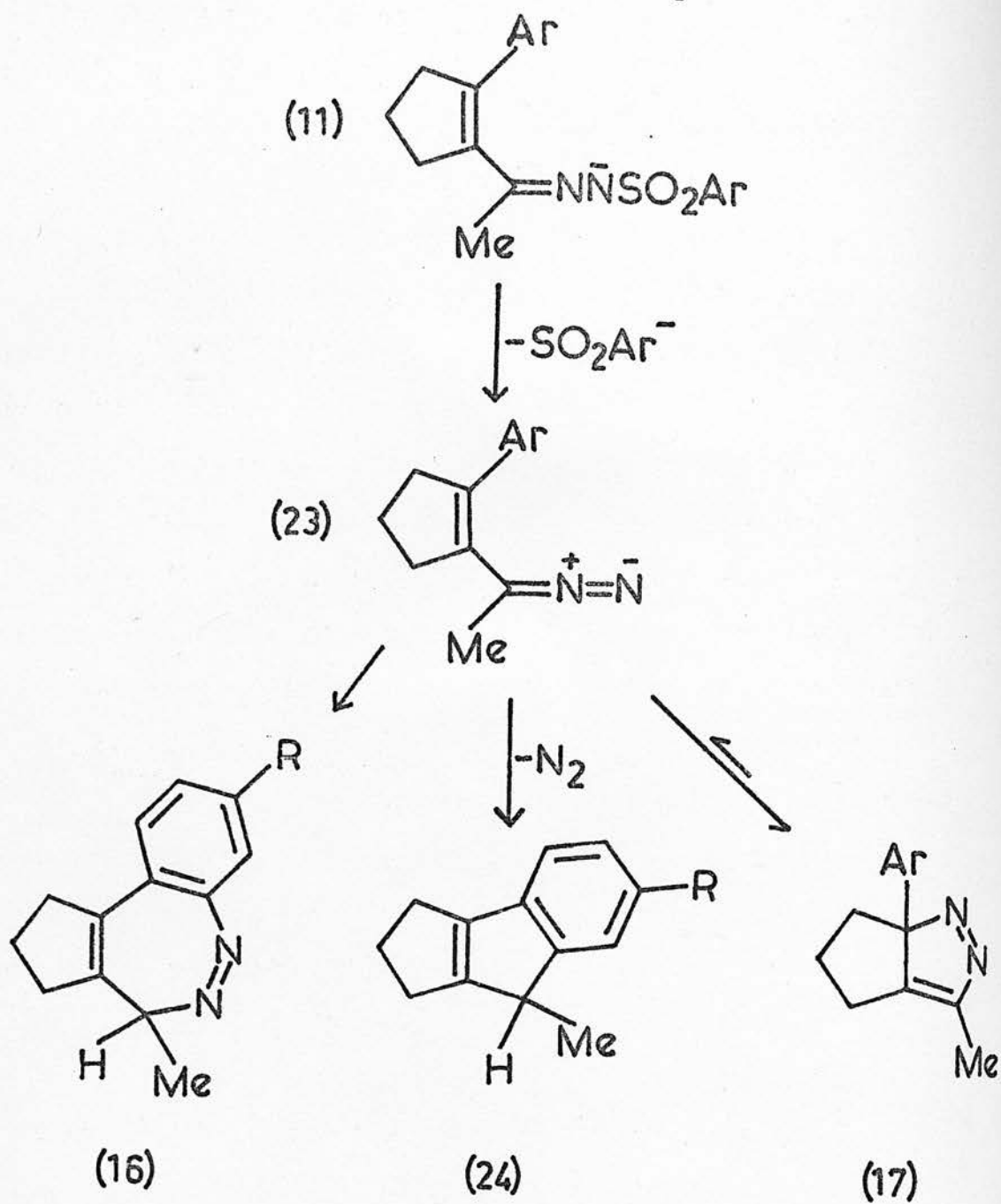
The 6a-aryl-4,5,6-trihydro-3-methylcyclopenta[c]pyrazoles (17) were heated under reflux in DME and were found to decompose to give both the indene (24) and the diazepine (16). Diazepine (16a) was found to be stable under these conditions. Tri-n-butylphosphine was again used to determine whether the 6 π -electron ring closure of diazoalkene (23) was reversible or whether the indene (24) and the diazepine (16) were formed from the 3H-pyrazole by a route other than via the diazoalkene, perhaps involving the diradical (41, scheme 4), or the formation of the diazepine (16) via a concerted 1,3-shift. The formation of a good yield of hydrazone (40) when the 3H-pyrazole (17a) was heated in DME in the presence of tri-n-butylphosphine, and the complete lack of indene (24) and diazepine (16a) in the reaction, indicate that the 3H-pyrazole (17) does indeed reverse to give the diazoalkene (23). Under the same conditions, diazepine (16a) was shown to be stable in the presence of tri-n-butylphosphine, indicating that the phosphazine (39) could not have been formed from the diazepine (16a).

The possibility that the phosphazine could be formed directly from the 3H-pyrazole was also discounted on the grounds that 4,5,6,7-tetrahydro-3-methyl-7a-phenylindazole (42) when heated under reflux in DME in the presence of tri-n-butylphosphine underwent its usual van Alphen



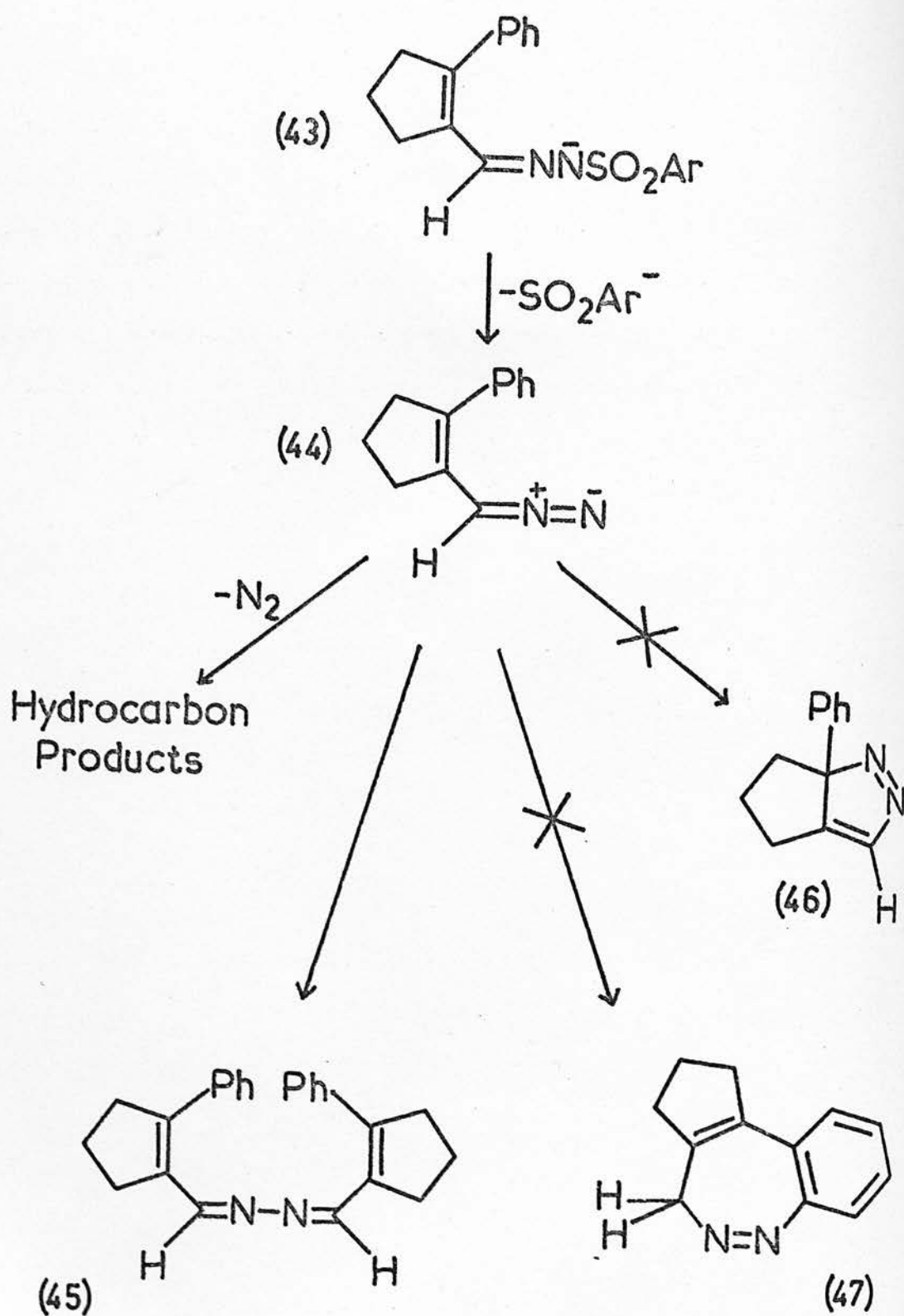
rearrangement (see later) and no phosphazine or hydrazone were formed.

The use of h.s.l.c. to monitor the decomposition of 1-acetyl-2-



Scheme 5

phenylcyclopentene tosylhydrazone (11a) showed that the initial rate of formation of the 3H-pyrazole (17) is much greater than the rate of formation of diazepine (16). Analysis of the reaction mixture after heating under reflux for 1.5 h showed that the ratio of 3H-pyrazole to diazepine was ca. 11 to 1. Only after this time when an appreciable amount of pyrazole had decomposed to give diazepine and indene, did the ratio of 3H-pyrazole to diazepine become smaller. Therefore the rate of pyrazole formation is faster, but the diazepine is the more thermodynamically stable product. The use of h.s.l.c. in the decomposition of 4,5,6-trihydro-3-methyl-6a-phenylcyclopenta[c]pyrazole (17a) indicated that the ratio of diazepine (16a) to indene (24a) was ca. 1 to 2. This ratio was confirmed by ¹Hn.m.r. spectroscopy of the crude product. However, the conditions of the dry column chromatography used to separate the products resulted in the decomposition of some of the indene. It is interesting that approximately half of the indene derived from the 3H-pyrazoles decomposed on a dry column during work-up, whereas no appreciable decomposition took place during the work-up of the products derived from the tosylhydrazones. There are two possible explanations for this: a) the aromatic solvents used in the former cases encouraged the decomposition, or b) the indene was washed off the alumina more quickly in the latter cases than in the former, resulting in less decomposition. Thus, after all this data has been assembled, it is possible to establish with some certainty the mechanism as shown in scheme 5. The similarity in the yields of indene and diazepine (scheme 2) from the three tosylhydrazones indicates that the substituent effects in the β -aryl group are minimal. This is in agreement with the lack of such substituent effects in the cyclisation of 1-aryl-3-diazopropenes to pyrazoles.¹³

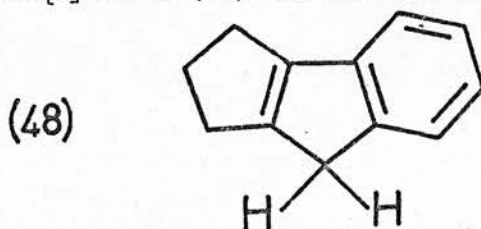


Scheme 6

3. 2-Phenylcyclopenten-1-al tosylhydrazone.

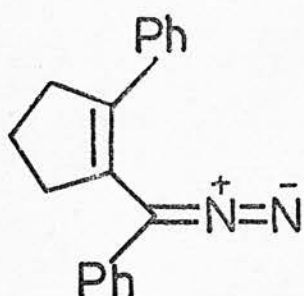
The sodium salt of 2-phenylcyclopenten-1-al tosylhydrazone (43) decomposed when heated in boiling DME to give a red-coloured mixture which indicated the presence of diazoalkene (44). After removal of the *p*-toluenesulphinate, the usual work-up gave a brown oil which contained a large number of compounds (scheme 6). This mixture was separated by dry column chromatography into two components and a small yield of 2-phenylcyclopenten-1-al azine (45, 5%) was crystallised from the component with the smaller *R_f*. The azine (45) was identified by its ¹Hn.m.r. spectrum which showed a low field aldehyde proton (τ 1.54) and its mass spectrum which had a molecular ion at *m/e* 340, which in addition to losing a hydrogen atom (*m/e* 339) readily broke the N-N single bond to form *m/e* 170. No other compound could be identified in the fraction of the product with the smaller *R_f*, but t.l.c. indicated that none of the products in the mixture were yellow coloured and mass spectrometry of this fraction indicated only very small peaks at *m/e* 184 (C₁₂H₁₂N₂) and *m/e* 156 (C₁₂H₁₂). These two facts strongly suggest that no pyrazole (46) or diazepine (47) was formed in the decomposition.

The component of the product which had a large *R_f* on dry column chromatography was examined by g.l.c. and g.l.c.-m.s. These techniques showed two volatile products in the ratio 6:1. The mass spectrum of the major peak had its base peak at *m/e* 156, and peaks at *m/e* 155 (44%) and *m/e* 128 (79%) which correspond to loss of .H and C₂H₄ from C₁₂H₁₂⁺. This data supports the structure of 1,2,3,4,4-pentahydro-cyclopenta[b]indene (48) but this structure could not be confirmed by

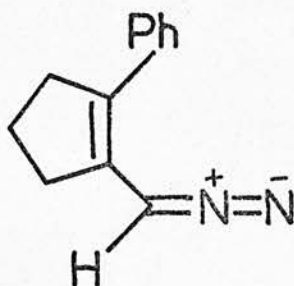


the $^1\text{Hn.m.r.}$ spectrum of the mixture.

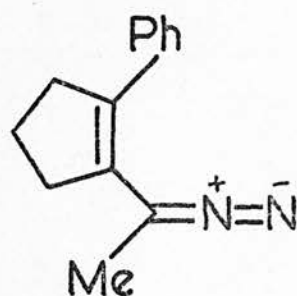
It is apparent, however, that in the decomposition of diazoalkene (44), carbene derived products (hydrocarbons and azine) predominate to the exclusion of pyrazole and diazepine. This is in agreement with the previous data on compounds of the same geometry round the π -system. Diazoalkene (8) is the most stable of (8), (44), and (23a),¹ and hence



(8)

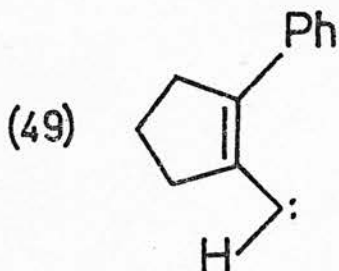


(44)

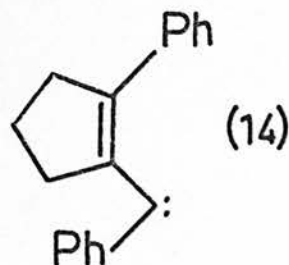


(23a)

cannot surmount the energy barriers which are necessary to form pyrazole and diazepine. The carbene from (8), however, is stable and hence provides a facile route to hydrocarbon products. Diazoalkene (23a) is the least stable of the three and is able to form a 3H -pyrazole and a diazepine. Diazoalkene (44) is more stable than (23a) and evidently does not readily attain the transition states which must be reached in order to form pyrazole and diazepine. However, the carbene (49) derived from (44) will be much less stable than that carbene (14) formed from (8), due to the conjugation of the additional



(49)

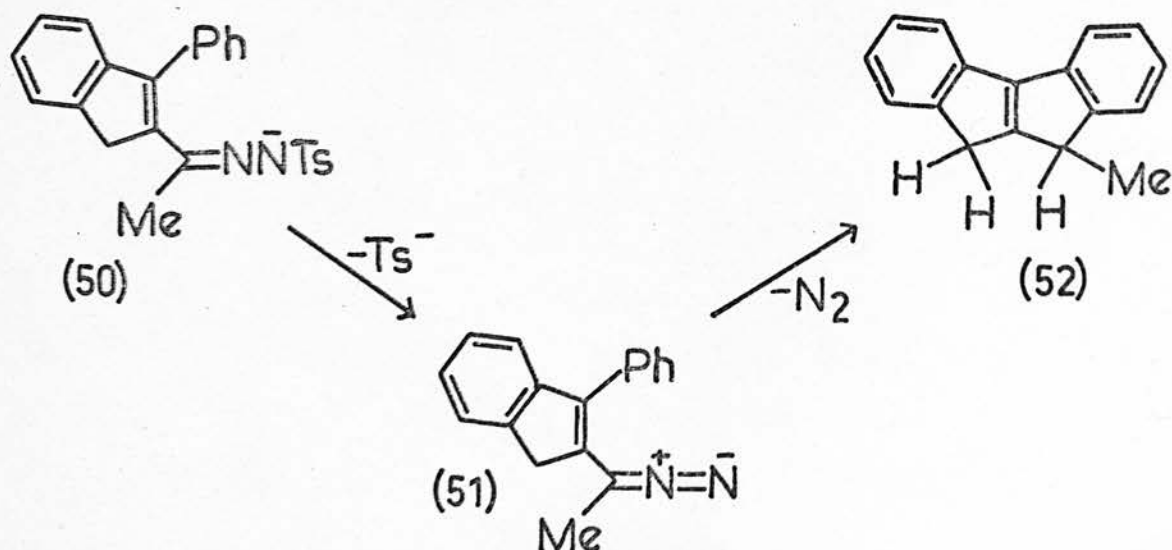


(14)

phenyl group in (14), and if that instability is manifested in a less easily attainable transition state between (44) and (49), then it is clear that the diazoalkene (44) does not have any facile mode of decomposition which is likely to result in a "clean" reaction. The products are partially derived from carbene (49), but it is apparent that a considerable amount of the diazoalkene (44) decomposes by unknown routes to give multiple, unidentified products.

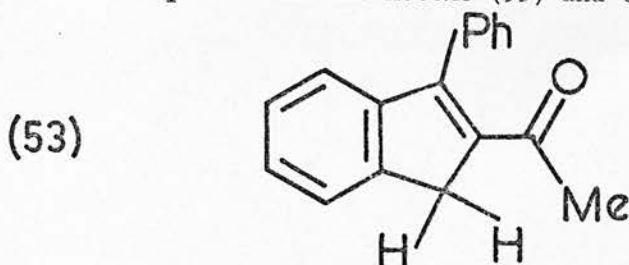
4. 2-Acetyl-3-phenylindene tosylhydrazone.

When heated under reflux in DME, the sodium salt of 2-acetyl-3-phenylindene tosylhydrazone (50) quickly decomposed to the diazoalkene (51), the presence of which was indicated by a red-brown coloration. Although all the tosylhydrazone had decomposed within 1 h, the reaction mixture was kept at 65° for a further 18 h to ensure the complete reaction of the diazoalkene. The usual work-up gave a solid which was purified by dry column chromatography to give 1-methylindeno-(2',3':2,3)indene (52, 72%). This hydrocarbon was identified by

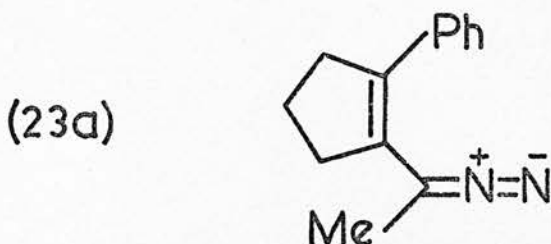


its 1H n.m.r. spectrum which showed a benzylic proton (τ 6.33,q,J 8Hz), a methyl group (τ 8.58,d,J 8Hz) and two equivalent benzylic protons (τ 6.45,s). The equivalence of the two benzylic protons is accidental

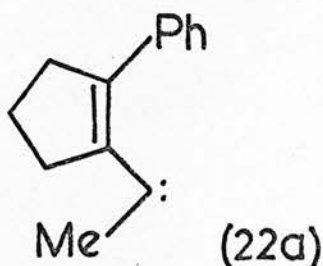
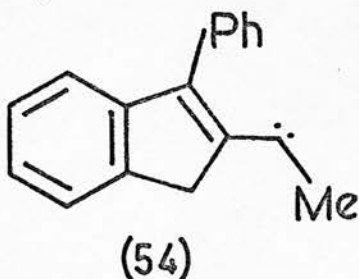
unlike the equivalence of the same two protons in the ketone (53) and the tosylhydrazone (50).



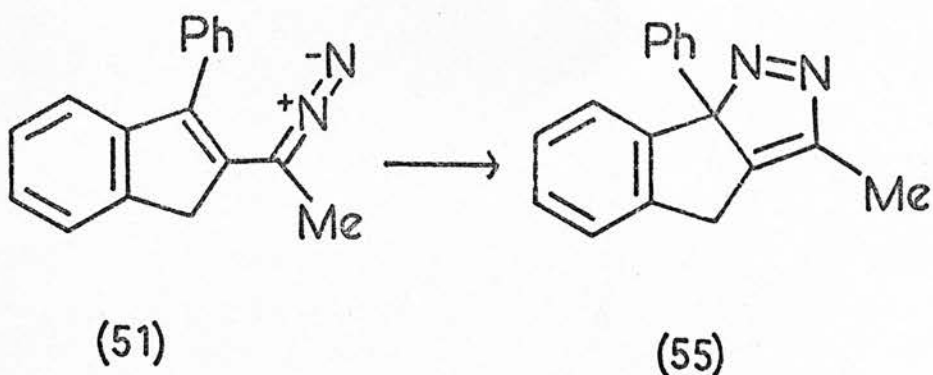
The molecular geometry of diazoalkene (51) around the π -system which would be involved in any 6π - or 8π -electron ring closure is virtually identical to that of diazoalkene (23a). It is possible



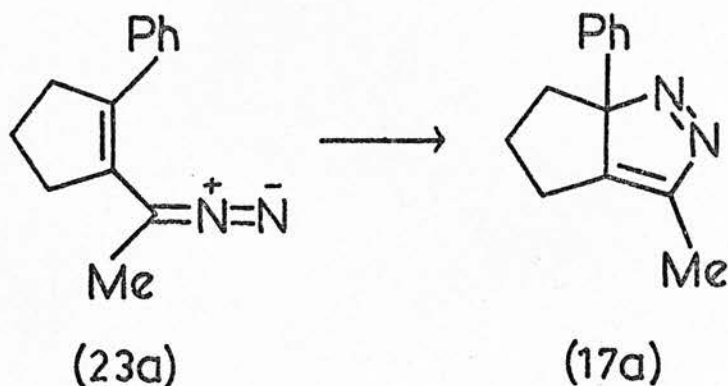
that the carbene (54) from diazoalkene (51) is more stable relative to its diazoalkene than is the carbene (22a) derived from diazoalkene (23a). This would be because of the increased delocalisation which



is possible through the additional aromatic ring in (54). This would account for the higher yield of hydrocarbon found in the decomposition of (51) compared to (23a). A contributing factor to the high yield of (52) may be that in order to form the $3H$ -pyrazole (55) from diazoalkene (51) would involve both the aromatic rings in (51) becoming non-conjugated with the rest of the π -system (and hence with each other). This is likely to make (51) to (55) a less favourable reaction

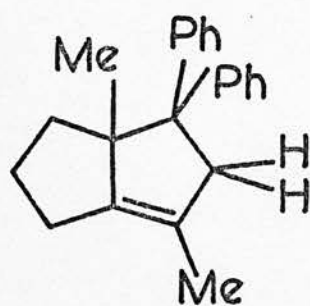
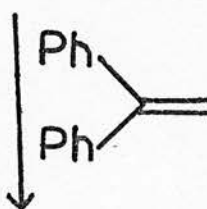
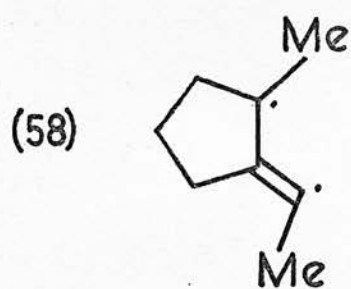
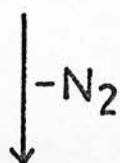
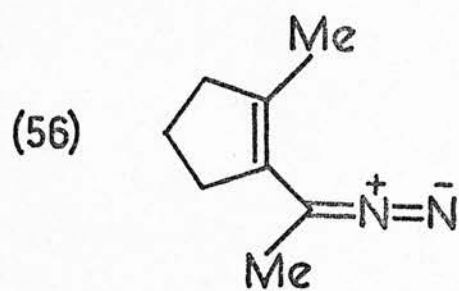


than (23a) to (17a) where only one phenyl group becomes non-conjugated

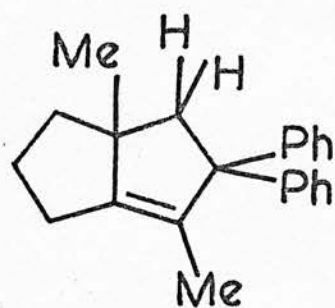


with the rest of the π -system. It is important to remember in this context that (23a) to (17a) is the kinetically favoured reaction in the decomposition of diazoalkene (23a).

The remainder of the decomposition product of diazoalkene (51) was a mixture of compounds which could not be identified, but which did not appear to contain any pyrazole or diazepine. It is also reasonably certain that no 3H-pyrazole was formed as a moderately long lived intermediate in the decomposition as no such material could be seen using t.l.c.



or



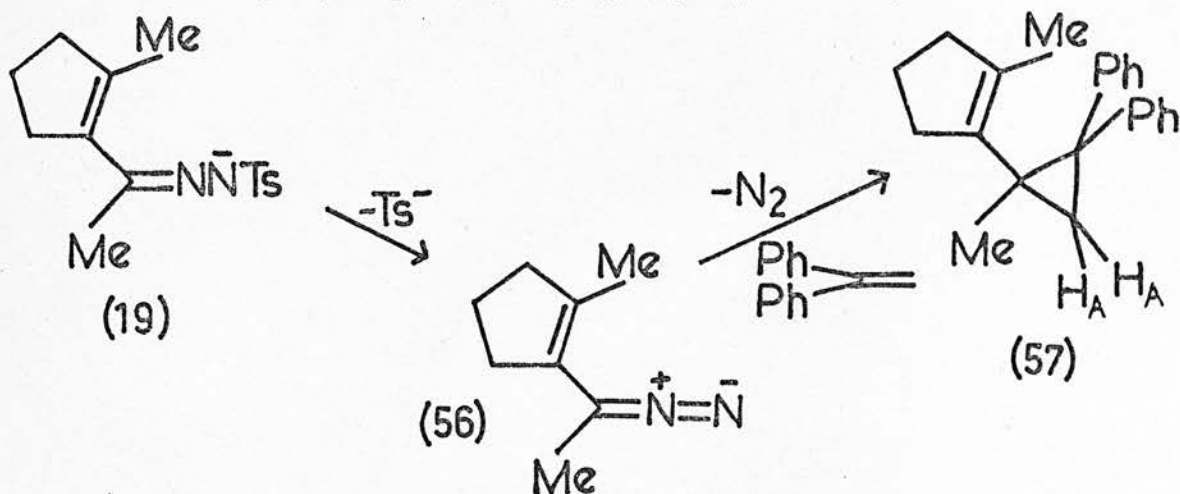
(59)

Scheme 7

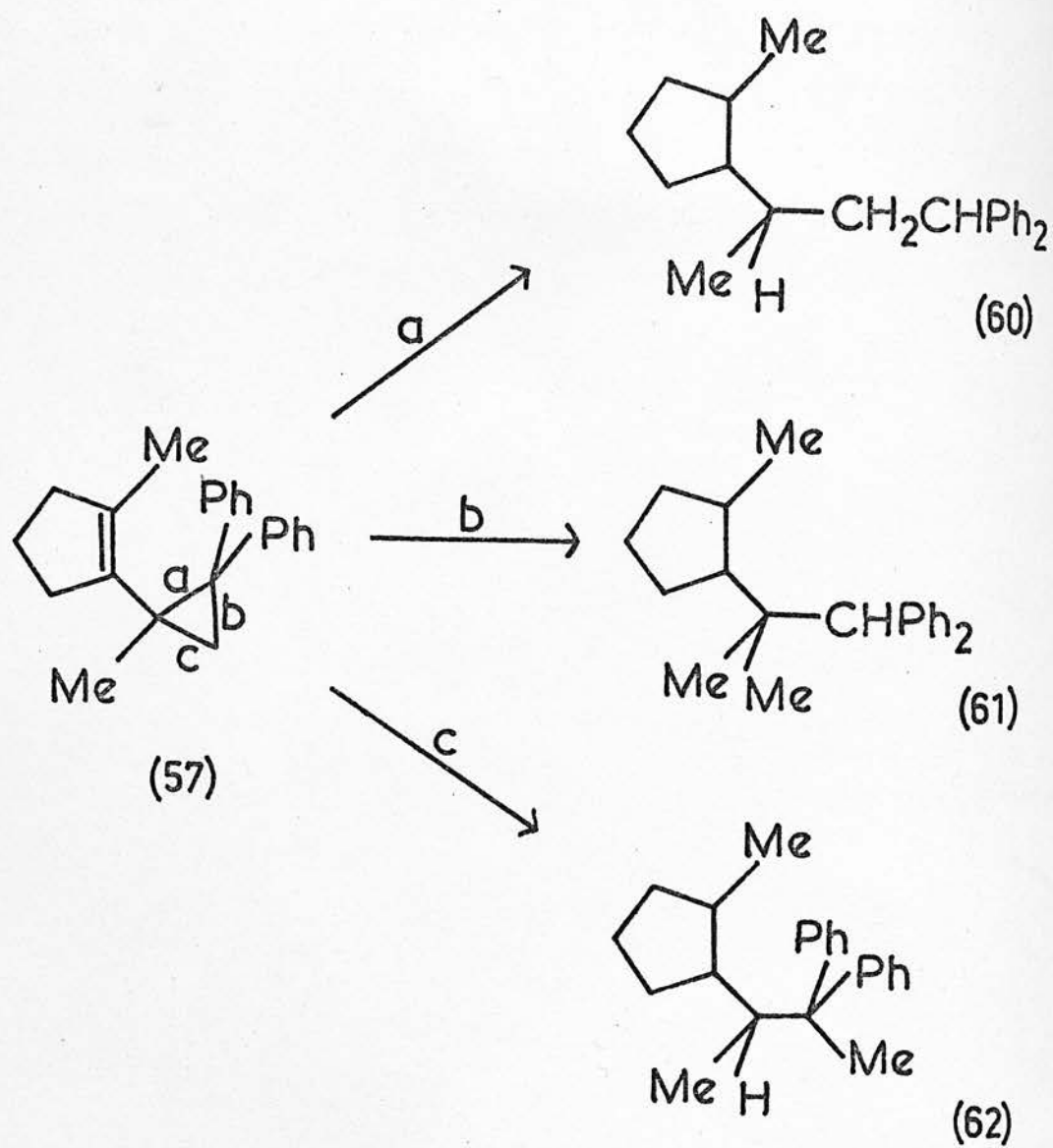
5. 1-Acetyl-2-methylcyclopentene tosylhydrazone.⁴³

The decomposition of the sodium salt of 1-acetyl-2-methylcyclopentene tosylhydrazone (19) resulted in the appearance of the red colour due to 1-(1-diazoethyl)-2-methylcyclopentene (56) which faded to give a yellow solution. T.l.c. and g.l.c. of the product indicated that multiple products, probably hydrocarbons, had been formed, but it was not possible to identify any of them.

Decomposition of the tosylhydrazone (19) in the presence of 1,1-diphenylethylene also gave a red solution, but in this case, the colour faded more quickly and analysis of the reaction mixture by g.l.c. indicated that only one g.l.c.-volatile product had been formed. Distillation, followed by dry column chromatography afforded 1-methyl-2-(1-methyl-2,2-diphenylcyclopropyl)cyclopentene (57). This adduct

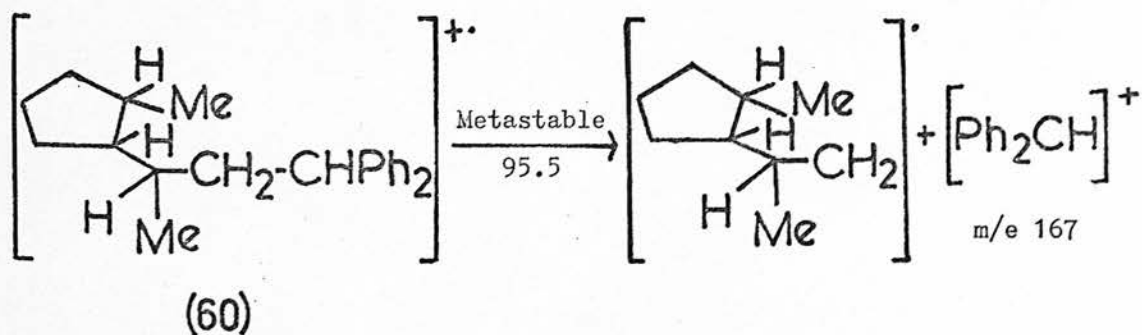


was identified by its mass and ^1H .m.r. spectra. The mass spectrum had a molecular ion (m/e 288) which readily lost a methyl group (m/e 273). The ^1H .m.r. spectrum showed that the pair of doublets (H_A) had small coupling constants (J 5Hz). Irradiation on either doublet caused collapse of the other. The small coupling constant is typical of geminal protons in cyclopropyl rings,^{87,99} and too small for geminal protons in larger rings. This rules out the possibility of the trapping of diradical (58) to give adduct (59, scheme 7).

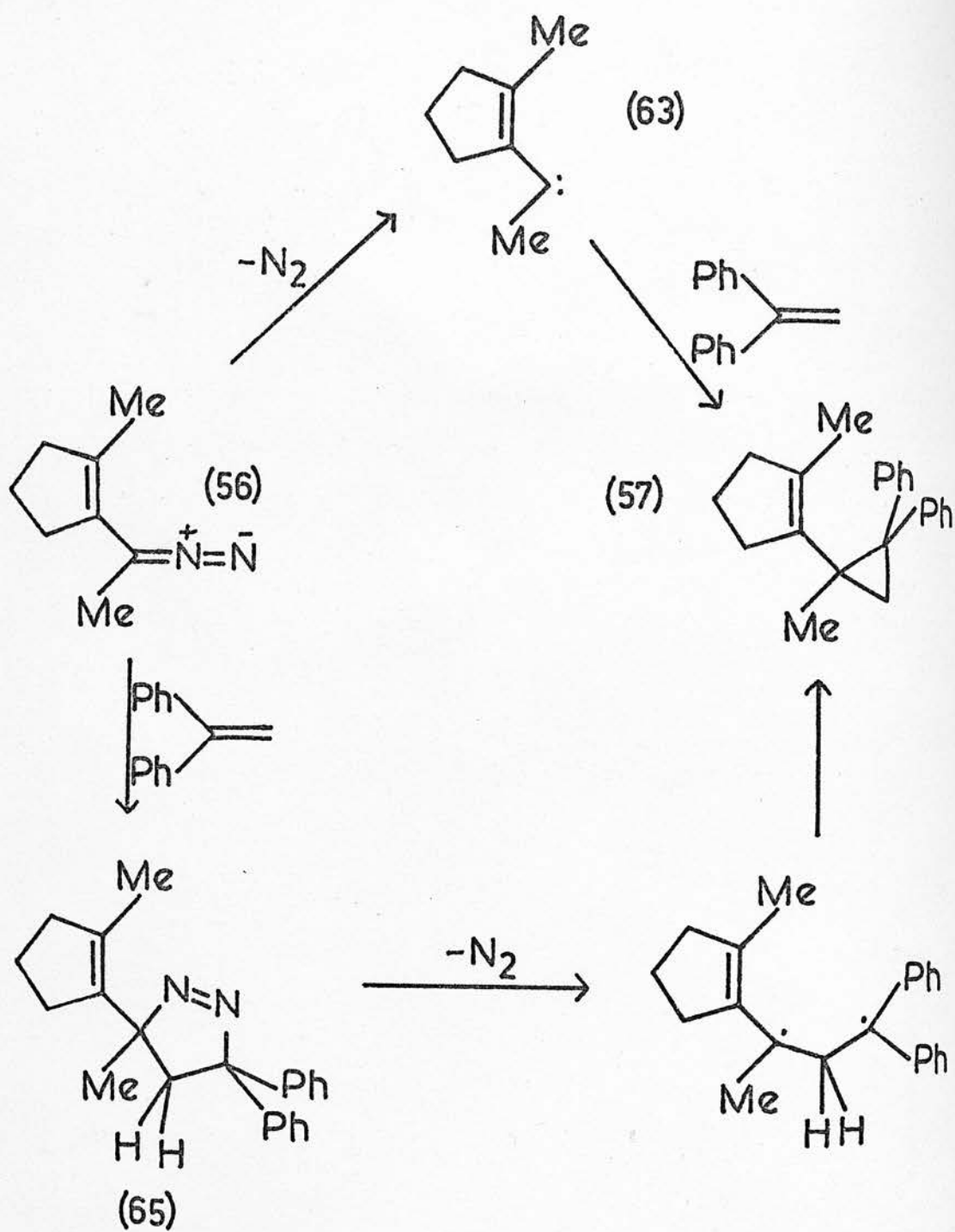


Scheme 8

The structure of adduct (57) was confirmed by its hydrogenation at atmospheric pressure during which two molecules of hydrogen were taken up per molecule of substrate. The resulting product was a mixture of hydrocarbons which could not be separated, but which could be partially identified by means of the $^1\text{Hn.m.r.}$ and mass spectra of the mixture. It is known¹⁰⁰ that phenyl or vinyl substituents in cyclopropane rings increase the ease with which the ring is broken. Hydrogenolysis of these compounds results in the breaking of that bond which is adjacent to the activating substituent. On such grounds it would appear that ring opening of (57, scheme 8) by route "a" (three activating substituents) would be favoured over route "b" (two activating substituents) which would be favoured over route "c" (one activating substituent). The spectra of the product bore out this prediction. The $^1\text{Hn.m.r.}$ spectrum had a benzylic multiplet (τ 5.8-6.1) which integrated for 0.8H. Thus, there appears to be much more (60) plus (61), than (62). This was confirmed by the mass spectrum which showed the molecular ion (m/e 292) losing $\cdot\text{C}_9\text{H}_{17}$ to leave the base peak at m/e 167. This can be achieved by either (60) or (61).

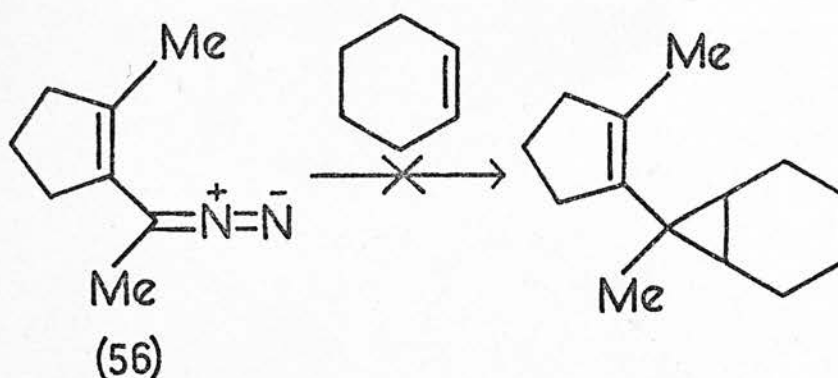


Unlike the quantitative yield of adduct (57) formed in the presence of 1,1-diphenylethylene, the decomposition of 1-acetyl-2-methylcyclopentene tosylhydrazone (19) in cyclohexene resulted in a large number of products, none of which could be identified. Extensive g.l.c.-m.s. research failed to show any compound with a molecular ion of m/e 190.

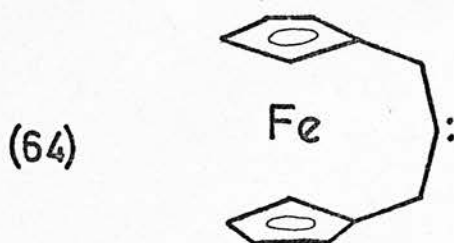


Scheme 9

Such an ion could have been attributed to the adduct of the carbene plus cyclohexene.



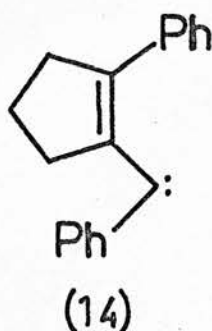
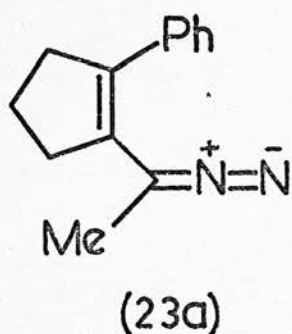
The most likely explanation of the behaviour of diazoalkene (56) with these olefins is that the carbene (63) quickly undergoes inter-system crossing from the singlet to the triplet state, in which state 1,1-diphenylethylene is a much more effective trap than cyclohexene.⁹¹ Moritani⁹⁰ used this argument to infer the triplet multiplicity of ferrocenophane- β -carbene (64) which added to 1,1-diphenylethylene, but not to dec-1-ene.



It is still open to some question whether adduct (57) is formed from carbene (63) or whether the diazoalkene (56) adds to the olefin to give pyrazoline (65) which then loses nitrogen to give the diradical (scheme 9). This latter mechanism could readily explain the lower concentration of diazoalkene (faster disappearance of red colour) found when the decomposition is carried out in the presence of 1,1-diphenylethylene. The olefin could quickly react with the diazoalkene (56), keeping its concentration low, whereas in the carbene mechanism

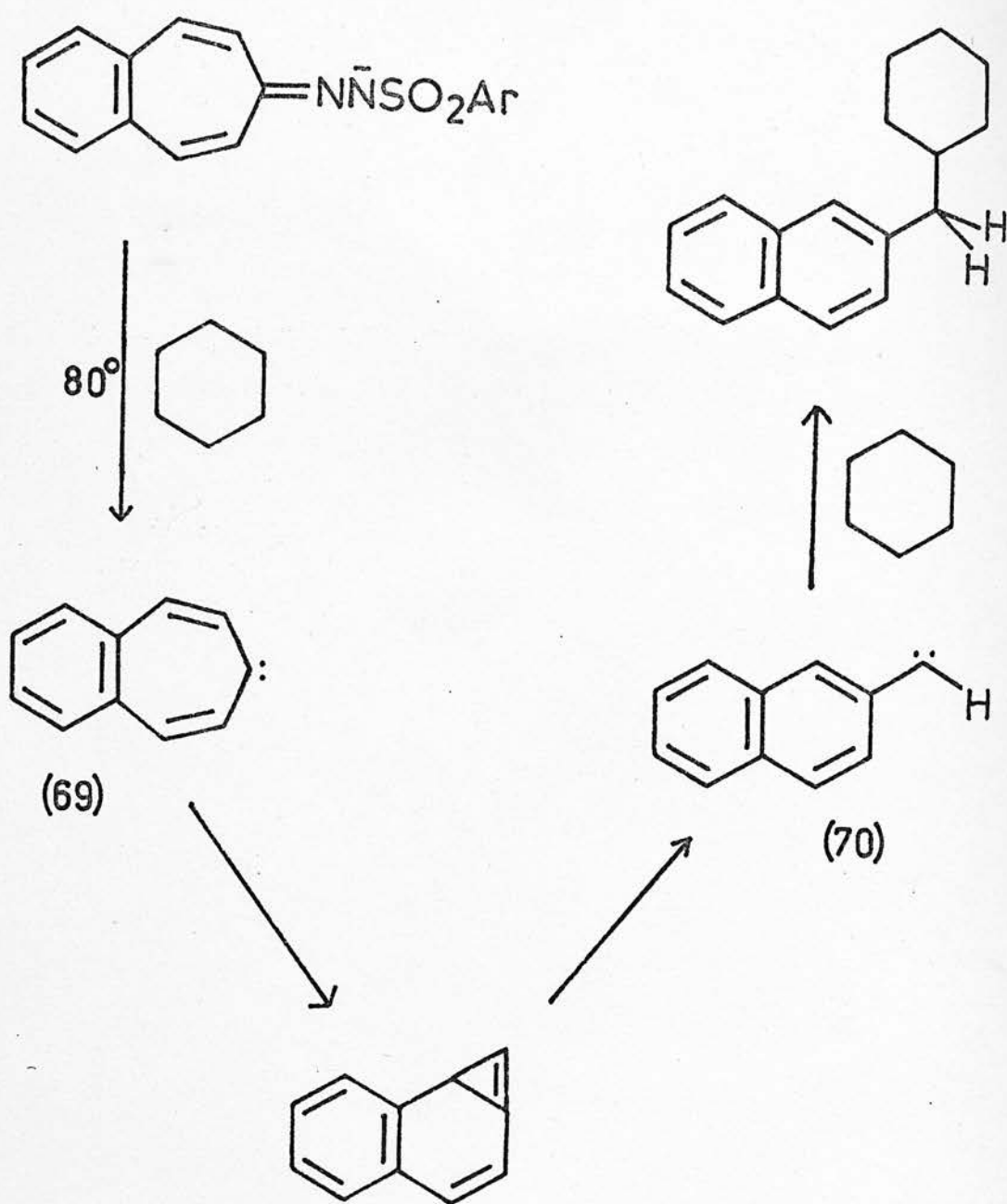
presumably the loss of nitrogen is the rate determining step, and hence should be independent of the olefin concentration. It seems likely, however, in view of the preferential trapping ability of 1,1-diphenylethylene compared to cyclohexene, and also because pyrazoline (65), if formed, would probably be stable under reaction conditions,¹⁰¹ that the diazoalkene (56) decomposed faster to the carbene (63) in the presence of 1,1-diphenylethylene because the reaction temperature in that case was rather higher than in the absence of the olefin.

It has already been argued that cyclisation of diazoalkenes with π -system geometry as in (56) do not readily undergo ring closure to the 3H-pyrazole because of the large distance between the ends of the 6π -system. Furthermore, diazoalkene (56) should cyclise more slowly¹³ to the 3H-pyrazole than does (23a) due to the different substituents on the β -carbon. Despite the fact that carbene (63) does not have

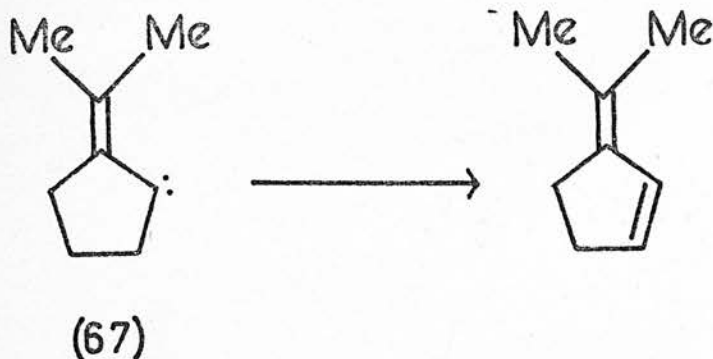


much conjugation to stabilize it (cf. 14) it appears from the products formed that the formation of (63) is the favoured mode of decomposition of diazoalkene (56).

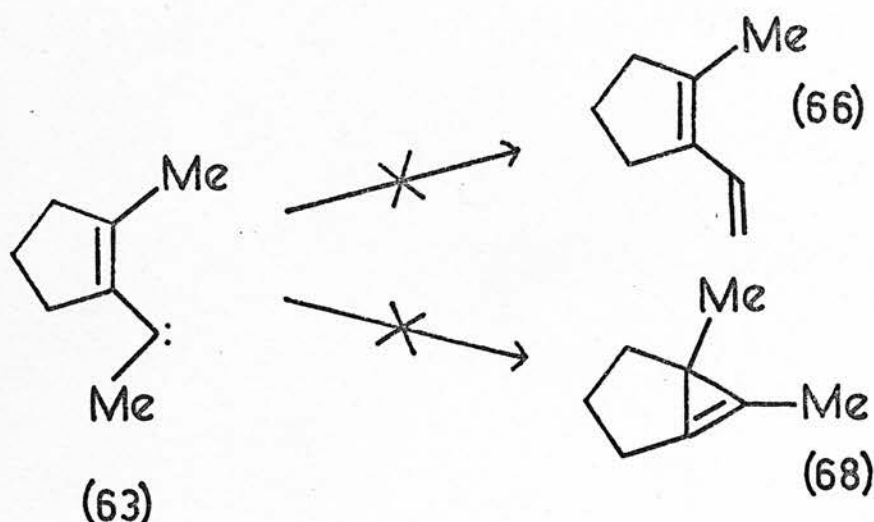
Let us now consider the possible reactions which are open to carbene (63). It might be able to undergo a hydrogen shift to give diene (66) as does 2-dimethylmethylenecyclopentylcarbene⁴⁰ (67), but this is apparently not favourable, probably because of the fast inter-system crossing of the first-formed singlet carbene to the triplet carbene which cannot readily react in this manner.¹⁰² The formation



Scheme 10



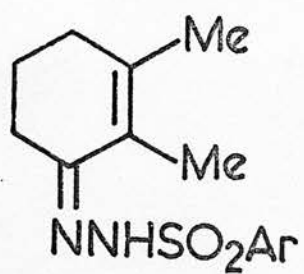
of bicyclic cyclopentene (68) as a stable product is most unlikely because of the strain involved in the fusion of the two rings. Thus



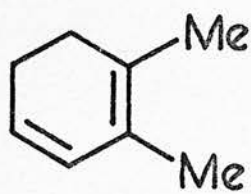
the most obvious intramolecular reaction modes are not facile routes to stable compounds for carbene (63). It is apparent that the carbene reacts in a variety of ways, perhaps involving intermolecular reactions, fragmentations, and molecular rearrangements.

The consideration of one possibility for the decomposition of carbene (63) was prompted by the reports^{24,25} of carbene-carbene rearrangements in conditions not dissimilar to those used in this research. For example, benzocycloheptatrienyliene (69) in boiling cyclohexane afforded a good yield (51%) of the insertion product of

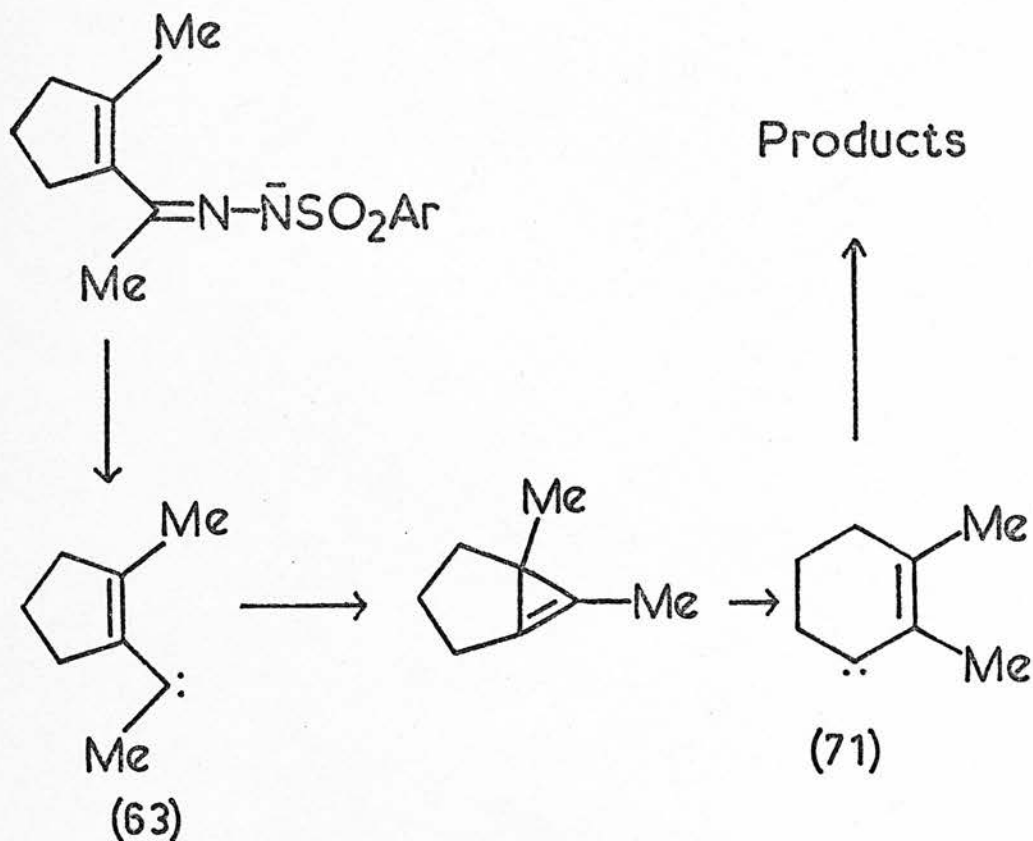
(72)



(73)

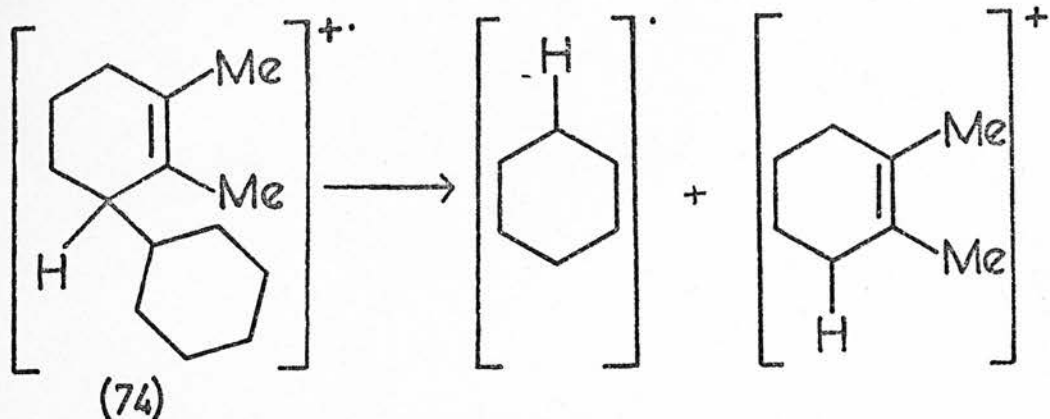


β -naphthylcarbene (70, scheme 10). If a similar mechanism is involved in the decomposition of 1-acetyl-2-methylcyclopentene tosylhydrazone, then products derived from 2,3-dimethylcyclohex-2-enylcarbene (71) would be formed. To this end, the sodium salt of 2,3-dimethylcyclohex-2-enone tosylhydrazone was decomposed.



6. 2,3-Dimethylcyclohex-2-enone tosylhydrazone.

The sodium salt of 2,3-dimethylcyclohex-2-enone tosylhydrazone (72) was heated under reflux in cyclohexane and analysis of the product solution by t.l.c. and g.l.c. indicated that many products had been formed. These products could not be separated, but g.l.c.-m.s. of the major peaks showed the presence of what were probably 1,2-dimethylcyclohexa-1,3-diene (73) which had a molecular ion at m/e 108 which lost a methyl group to give the base peak at m/e 93, and 3-cyclohexyl-1,2-dimethylcyclohexene (74) which lost $\cdot C_6H_{11}$ from its molecular ion at m/e 192 to give the base peak at m/e 109.

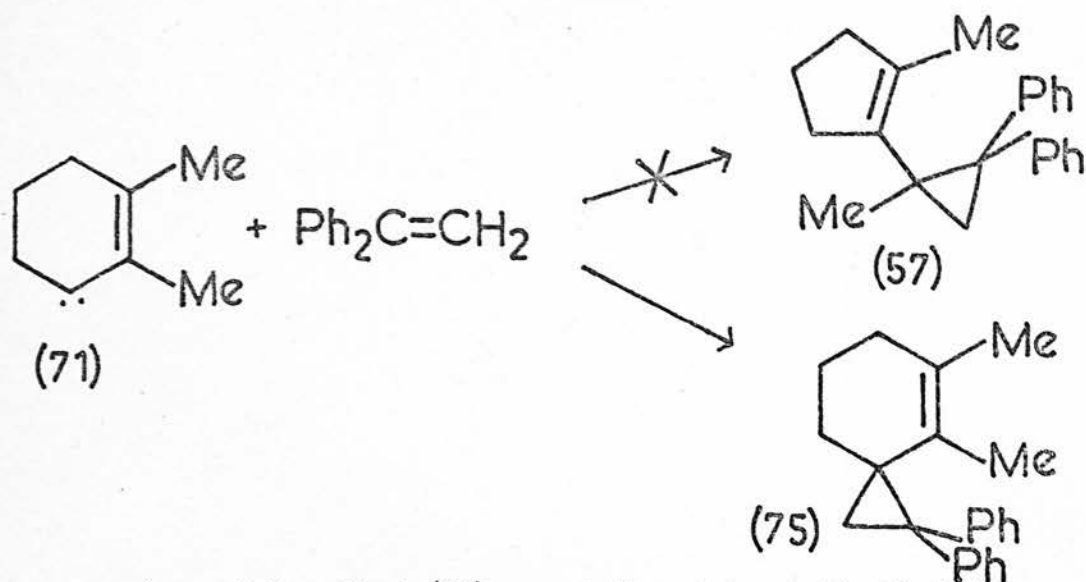


Products (73) and (74) are both predictable. Kirmse¹⁴ says that β -C-H insertion to give an olefin occurs almost exclusively when the divalent carbon is incorporated in five- and six-membered rings.

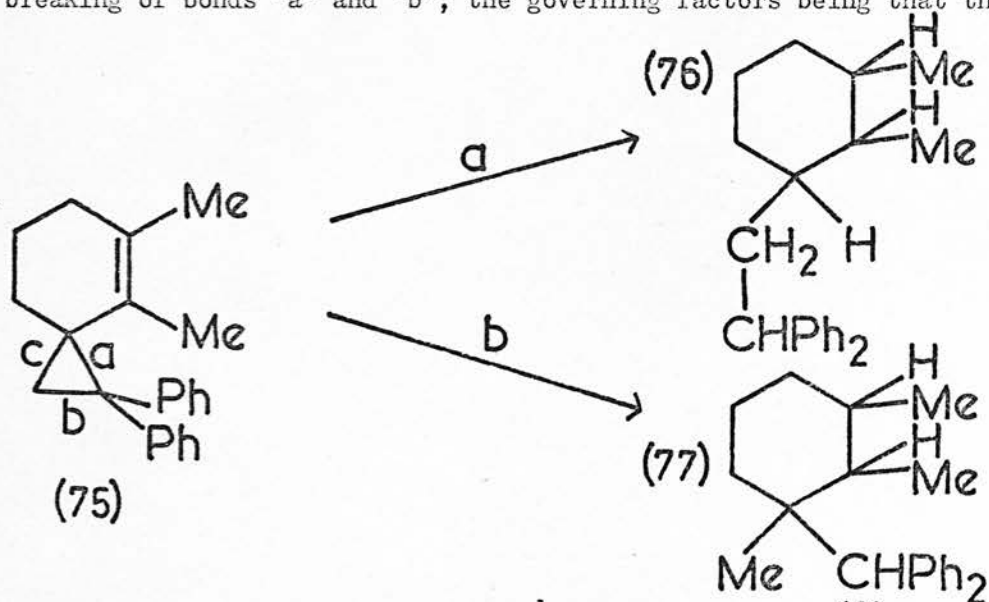
One further interesting mass spectrum was taken from the product mixture. This had a molecular ion at m/e 154, and although it was not found possible to identify the compound, the spectrum was identical with spectra obtained by Stanley⁴³ in the decomposition of 1-acetyl-2-methylcyclopentene tosylhydrazone in *p*-xylene and *n*-heptane. This was the only evidence which indicated the possibility of carbene-carbene rearrangement, and it was unfortunate that more time could not be devoted to investigating this possibility,

In order to ascertain if the cyclohexenyl carbene (71) would give the same adduct as the cyclopentenyl carbene (63), the decomposition of the tosylhydrazone salt (72) was carried out in the presence of 1,1-diphenylethylene. The decomposition occurred more quickly in the presence of the olefin, no doubt as a result of the higher reaction temperature. Examination of the product by g.l.c.-m.s. revealed two main products. The one with the shorter retention time was the mysterious compound with the molecular ion at m/e 154, and at the longer retention time was an adduct (M^+ 288) which, from its retention time and cracking pattern was not 1-methyl-2-(1-methyl-2,2-diphenylcyclopropyl)cyclopentene (57). Isolation of the pure product by dry

column chromatography and distillation allowed it to be identified as 2,3-dimethylcyclohex-2-enspiro-2',2'-diphenylcyclopropane (75). The

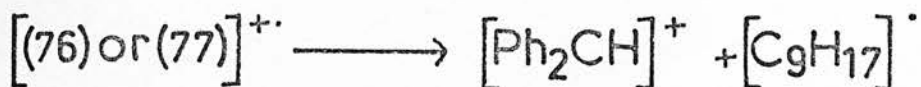


mass spectrum of the adduct (75) was similar, but not identical to that of (57) and its ^1H .m.r. spectrum showed the geminal constant (J 5Hz) typical of cyclopropanes.⁹⁹ The identity of the compound was confirmed by its hydrogenation product. The expected products from the hydrogenation/hydrogenolysis of (75) are those which involve the breaking of bonds "a" and "b", the governing factors being that the



bond which breaks should be adjacent to the vinyl group,¹⁰⁰ the phenyl groups,¹⁰⁰ and opposite to the spiro atom.¹⁰³ The mass spectrum of the product had its base peak at m/e 167, which indicates a

benzylic proton. The ^1H .m.r. spectrum indicated that all the product

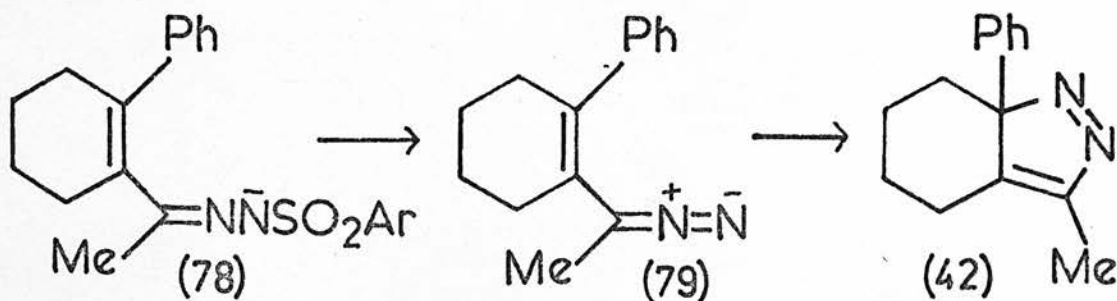


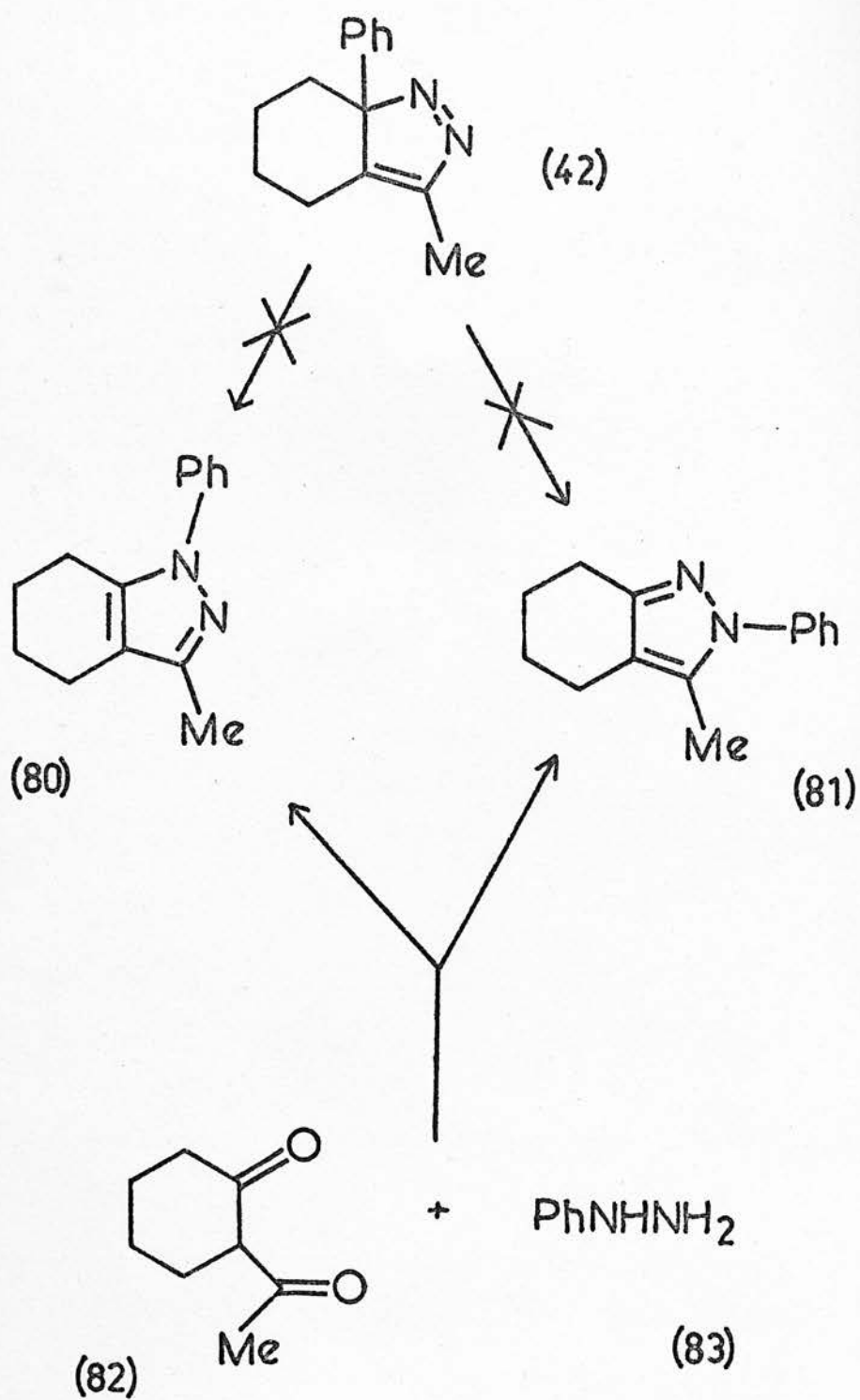
molecules had benzylic protons (τ 5.8–6.1, m, 1H), and the presence of a singlet (τ 8.58) which integrated for 1.5 protons (the methyl group in (77)), showed that approximately equal quantities of (76) and (77) had been formed.

7. 1-Acetyl-2-phenylcyclohexene tosylhydrazone.

In order to determine the effect of carbocyclic ring size on the decomposition of 1-(1-diazoethyl)-2-phenylcycloalkenes, the sodium salt of 1-acetyl-2-phenylcyclohexene tosylhydrazone (78) was decomposed in boiling DME. By analogy with the decomposition of 1-acetyl-2-phenylcyclopentene tosylhydrazone (11a), and considering the proximity of the ends of the 6 π -system in (79) compared to (23a), it seemed most likely that the kinetically favoured product would be 4,5,6,7-tetrahydro-3-methyl-7a-phenylindazole (42). It was of interest to find out if the indazole (42) would ring-expand to the diazepine as the analogous pyrazole (17a) had done, or if another mode of reaction would take place.

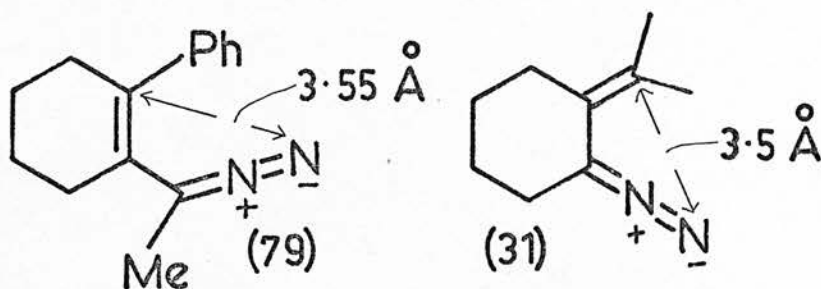
The tosylhydrazone decomposition did indeed give a virtually quantitative yield of indazole (42) after 4 h. At no state in the decomposition did a red colour develop, and hence it can be inferred that diazoalkene (79) never reached a high concentration. Only a moderate yield (33%) of the indazole was isolated by wet column





Scheme 11

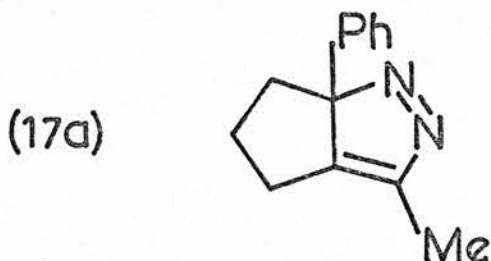
chromatography and recrystallisation, because the indazole slowly decomposed on the alumina. It is virtually certain, however, from t.l.c. and h.s.l.c. evidence, that the yield of indazole before work-up was very high. This fact is to be expected from the molecular geometry of the diazoalkene (79), which allows cyclisation to the 3H-pyrazole because of the short distance (3.55 Å) between the ends of the 6 π -system. This distance is virtually as short as that between the ends of the π -system in the 1-diazo-2-methylenecyclohexenes (31) which react exclusively to form pyrazoles.^{40,81}



The indazole (42) was identified by its ^1H and ^{13}C n.m.r. and mass spectra, as well as by comparison with isomeric compounds. It had been thought possible that the indazole (42), if formed, could undergo a van Alphen rearrangement⁴⁵ to one of the aromatic N-phenylindazoles (80) or (81), and to examine this possibility, a mixture of (80) and (81) was synthesised by the condensation of 2-acetylcyclohexanone (82) with phenylhydrazine (83, scheme 11).^{67,68} Comparison of the spectra of (80) and (81) with those of (42) showed that the product of cyclisation of diazoalkene (79) was neither (80) nor (81).

The mass spectrum of indazole (42) showed the molecular ion at m/e 212 (18%) losing nitrogen to give m/e 184 (48%) followed by the loss of a methyl group. The loss of nitrogen to give a much bigger peak than the parent is very good evidence for an azo group, and the spectrum of (42) is in good agreement with that of 4,5,6-trihydro-3-

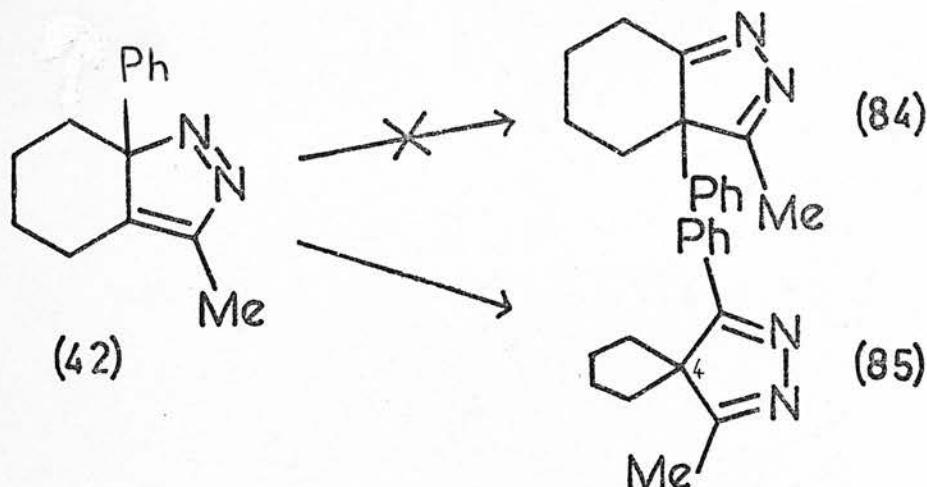
methyl-6a-phenylcyclopenta[c]pyrazole (17a), although the ratio $M-28^+ : M^+$ is much greater in (17a) which has greater ring strain than (42).



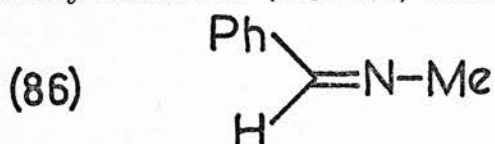
The $^1\text{Hn.m.r.}$ spectrum of (42) is not very informative, but the $^{13}\text{Cn.m.r.}$ spectrum confirmed its identity. C-7a, at 99.8 p.p.m. was in the region expected for a carbon in the 3H- position of a 3H- pyrazole, albeit rather less deshielded than in the case of the cyclopentane analogue (17a). All other carbons (aliphatic, olefinic and aromatic) appeared as sharp signals at their expected shift from TMS, and the spectrum is in excellent agreement with those of analogous tetrahydro- 3H- indazoles (see experimental Appendix 8).

When 4,5,6,7-tetrahydro-3-methyl-7a-phenylindazole (42) was heated for a long period (5 days) in DME, it did not ring expand to a benzodiazepine like (17), but instead slowly rearranged to an isomeric pyrazole. When the spectra of this product enabled the structures (80) and (81) to be discounted, it was assumed that the isomer was 4,5,6,7-tetrahydro-3-methyl-3a-phenylindazole (84), a structure which seemed to account for the $^1\text{Hn.m.r.}$ and mass spectra. It has been shown (see Introduction) that under normal circumstances aryl groups migrate more readily than alkyl groups in van Alphen rearrangements. The $^{13}\text{Cn.m.r.}$ spectrum, however, indicated that structure (84) was incorrect, because only two signals (each from two carbons) were found from the four CH_2 groups in the carbocyclic ring. Thus, barring accidental coincidence, which is most unlikely in the sharp lines of the spectrum, there must be only two types of carbon in the carbocyclic ring of the isomeric pyrazole. Thus, the structure is that of

3-methyl-5-phenyl-4-spirocyclopentane (85). The mass spectrum of



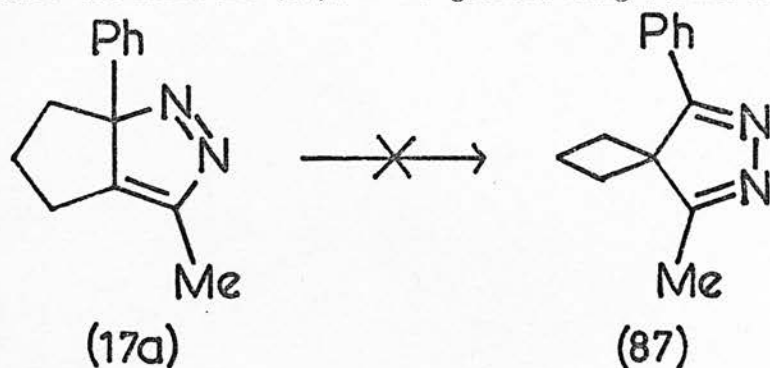
(85) had the molecular ion at m/e 212 (27%) losing 28 mass units to give m/e 184 (34%) followed by the loss of a methyl group. The peak at m/e 184 is mainly (but not entirely) due to loss of nitrogen, but it is only marginally larger than the parent ion, a fact which makes the presence of an azo group most unlikely, yet shows that the nitrogen atoms are bound together. The ^1H .m.r. spectrum showed two highly deshielded aromatic protons (τ 2.0-2.3) which are explained by the deshielding effect of the $\text{C}=\text{N}$ bond on the ortho-protons. This is analogous to the spectrum of (86)¹⁰⁴ which has the ortho-protons significantly deshielded (τ 2.2-2.4) from the rest (τ 2.55-2.75).



The ^{13}C .m.r. spectrum of 4H-pyrazole (85) had two highly deshielded signals at 178 and 181 p.p.m. which are attributed to the $\text{C}=\text{N}$ carbons. Such carbons are known⁹⁶ to have very low field signals. C-4 absorbed at 68 p.p.m. which agrees well with other 4H-pyrazoles.⁹⁶

The reason why the spiro-4H-pyrazole (85) is formed rather than (84) when previous work^{39,40,46} has indicated that alkyl groups migrate less readily than aryl ones is not easily explained. The precise mechanism of the thermal van Alphen rearrangement is not yet known,

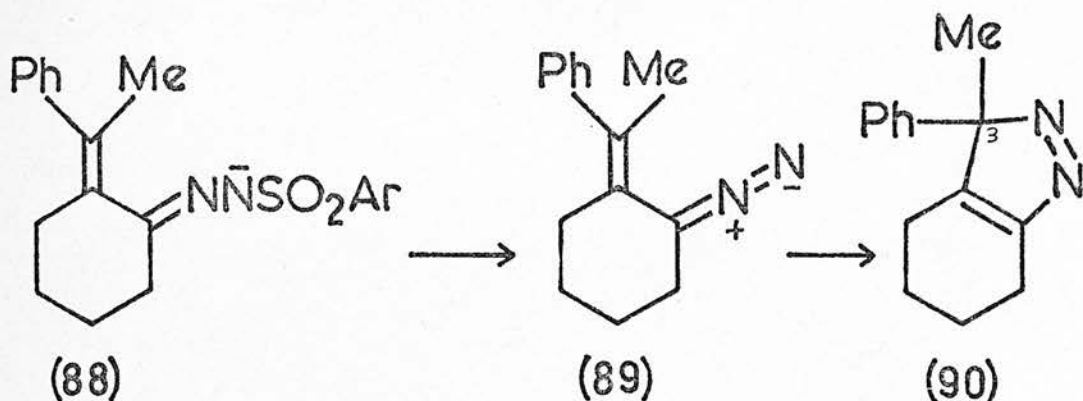
and indeed no one has proposed a reason why aryl groups normally migrate more readily than alkyl ones. It may be because of the relief of ring strain in (42) caused by the fusion of the five- and six-membered rings in a manner which includes adjacent sp^3 and sp^2 hybridised carbons which causes the anomalous alkyl shift to give the 4H-pyrazole (85). It is apparent that 4,5,6-trihydro-3-methyl-6a-phenylcyclopenta[c]pyrazole (17a) cannot undergo an analogous van Alphen rearrangement as this would introduce a strained cyclobutane ring into the molecule (87). The greater ring strain in (17a)



compared to (42) is the main reason why the former, and not the latter, is able to ring expand to the diazepine.

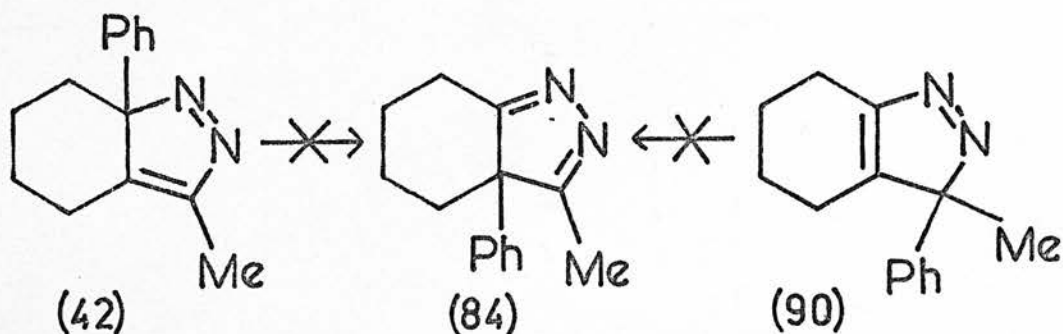
8. 2-(cis-Methyl-trans-phenylmethylene)cyclohexanone tosylhydrazone.

The sodium salt of the tosylhydrazone (88) was heated under reflux in DME for 30 h. After heating for a few minutes, a very pale pink colour was seen, but this quickly faded, indicating that the intermediate diazoalkene (89) never reached a high concentration. H.s.l.c. and t.l.c. showed the formation of one major product, which was worked-up and purified by wet column chromatography and recrystallisation to give 4,5,6,7-tetrahydro-3-methyl-3-phenylindazole (90, 58%). The yield was lowered considerably because the indazole slowly decomposed on alumina. The formation of (90) is predictable in the light of the formation of pyrazoles from analogous diazoalkenes.^{40,81}

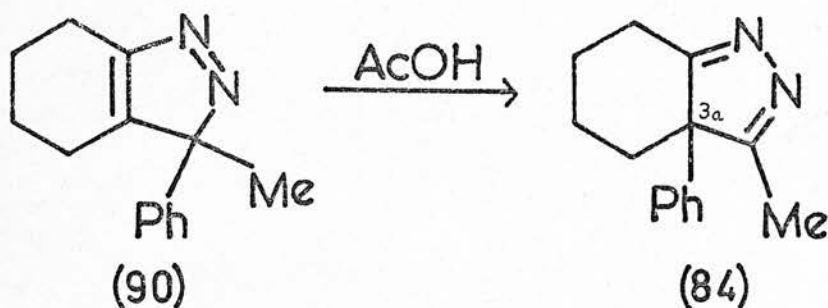


Indazole (90) was identified by its mass and n.m.r. spectra. The molecular ion at m/e 212 (16%) lost 28 mass units, almost entirely by loss of nitrogen to give m/e 184 (79%). The cracking pattern was very similar to that of indazole (42). The ^1H n.m.r. spectrum was not very informative, but agreed with the proposed structure, and the ^{13}C n.m.r. spectrum confirmed the identity. C-3 absorbed at 97 p.p.m. and the spectrum was in excellent agreement with those of other 3H-indazoles (see experimental Appendix 8).

The thermolysis of indazole (90) did not result in the formation of an isomeric pyrazole. When sufficiently hot solutions were used to decompose (90) multiple products were found which could not be identified. It is interesting to note that the product which would be predicted⁵¹ is precisely the compound (84) which was expected, but which did not form, in the thermolysis of 4,5,6,7-tetrahydro-3-methyl-7a-phenylindazole (42).



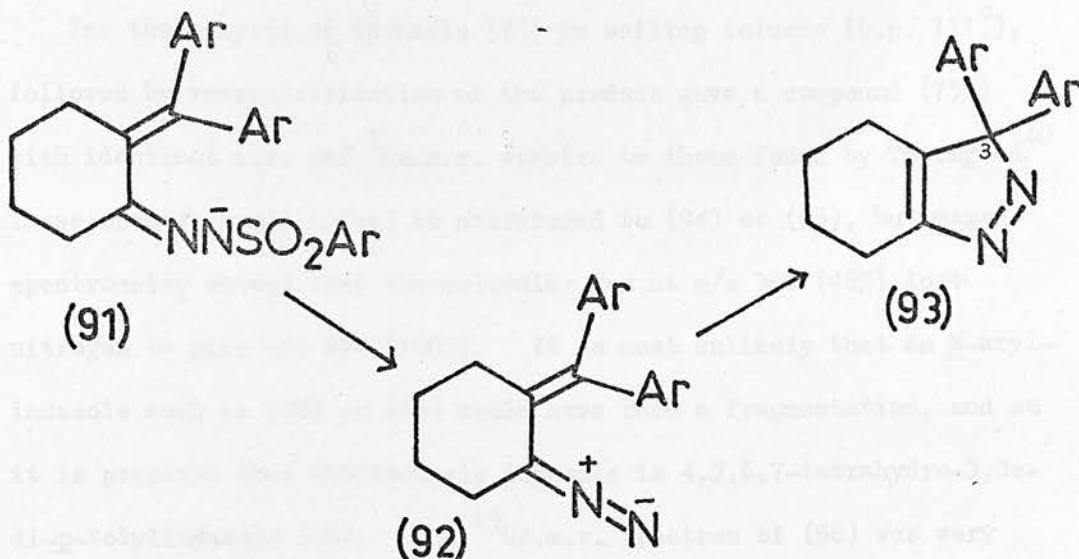
However, the treatment of indazole (90) with acetic acid at 95° resulted in a moderate yield (34% isolated) of 4,5,6,7-tetrahydro-3-methyl-3a-phenylindazole (84) which was identified by its mass and n.m.r. spectra as well as by comparison with isomeric compounds. The ^1H n.m.r. spectrum had an aromatic multiplet with no particularly



deshielded protons, indicating the absence of a $\text{Ph}-\text{C}=\text{N}-$ group.¹⁰⁴ The mass spectrum had a molecular ion at m/e 212 (26%) which lost nitrogen to give m/e 184 (23%). The M^+ : M^+-28 ratio indicates a $=\text{N}-\text{N}=$ system rather than a $-\text{N}=\text{N}-$. The ^{13}C n.m.r. spectrum of indazole (84) showed C-3a at 63.3 p.p.m. and two heavily deshielded $\text{C}=\text{N}$ signals (180 and 182 p.p.m.); these and other signals being in good agreement with the spectra of other 4H-pyrazoles (experimental Appendix 9). It can be concluded that (84) is only formed by van Alphen rearrangement from a 3H-pyrazole if vigorous acidic conditions are used.

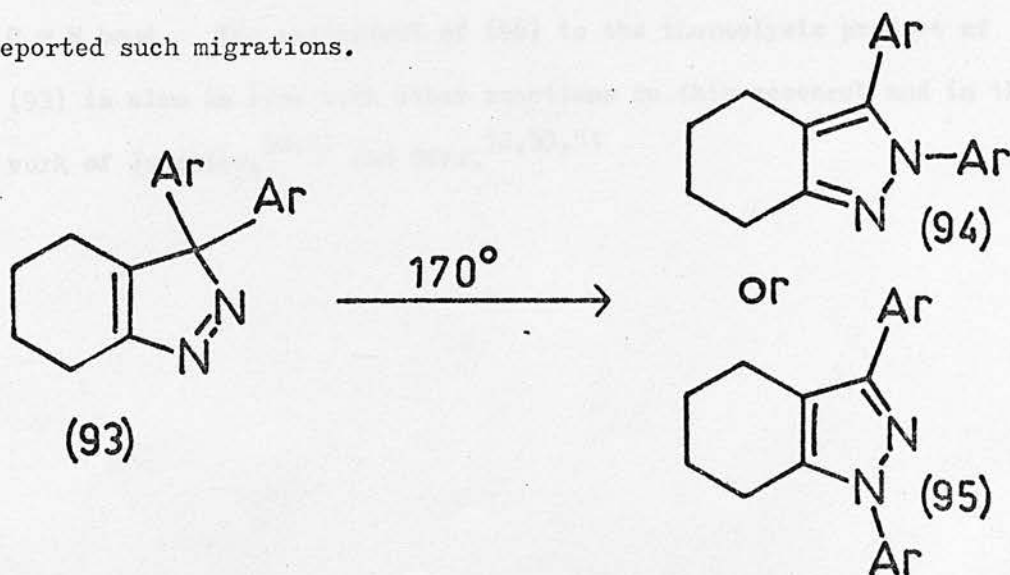
9. 2-(Di-p-tolylmethylene)cyclohexanone tosylhydrazone.⁴⁰

The sodium salt of the tosylhydrazone (91) was decomposed in DME. At no stage during the reaction did any red colour develop, hence it may be assumed that the diazoalkene (92) readily cyclised to the product. The usual work-up, followed by dry column chromatography and recrystallisation afforded 4,5,6,7-tetrahydro-3,3-di-p-tolylindazole (93). As with other 1-diazo-2-methylenecyclohexanes, the 6 π -electron ring closure of (92) to the 3H-indazole is a facile mode of decomposition because of

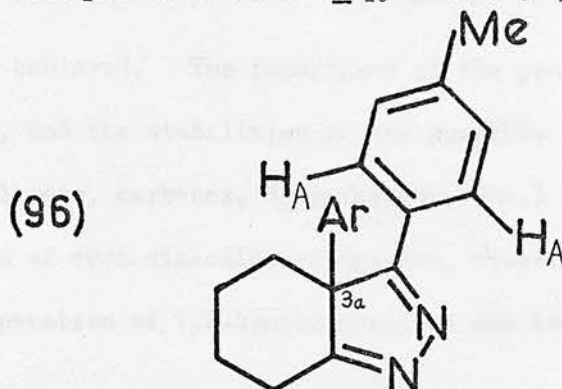


the short distance between the ends of the π -system. The melting point, i.r. and $^1\text{Hn.m.r.}$ spectra of the indazole (93) agreed with those of Thorogood.⁴⁰ The $^{13}\text{Cn.m.r.}$ spectrum showed the characteristic C-3 absorption at 104 p.p.m., and was in excellent agreement with the spectra of other tetrahydro-3H-indazoles (see experimental Appendix 8). The mass spectrum, which also agreed well with analogous compounds, had a small molecular ion at m/e 302 (8%) and an M^+-28 base peak which corresponded to loss of nitrogen, hence confirming the azo group.

Thorogood⁴⁰ pyrolysed the indazole (93) in a vacuum at 170° and obtained an isomeric compound to which he tentatively assigned the structure of an N-arylidazole (94) or (95) on the grounds of its i.r. and $^1\text{Hn.m.r.}$ spectra, as well as on the data of Hüttel⁴⁶ who had reported such migrations.



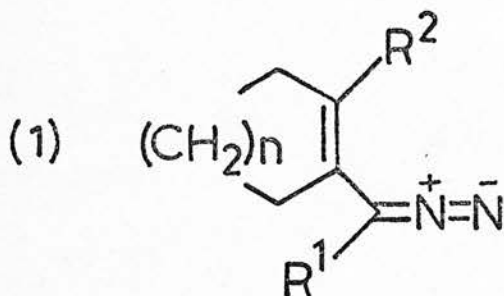
The thermolysis of indazole (93) in boiling toluene (b.p. 111°), followed by recrystallisation of the product gave a compound (75%) with identical i.r. and ^1H .m.r. spectra to those found by Thorogood.⁴⁰ These spectra could indeed be attributed to (94) or (95), but mass spectrometry showed that the molecular ion at m/e 302 (48%) lost nitrogen to give m/e 274 (100%). It is most unlikely that an N-aryl-indazole such as (94) or (95) could have such a fragmentation, and so it is proposed that the isomeric indazole is 4,5,6,7-tetrahydro-3,3a-di-p-tolylindazole (96). The ^{13}C .m.r. spectrum of (96) was very similar to the spectra of other 4H-pyrazoles (experimental Appendix



9), notable signals being C-3a at 67 p.p.m. and the two C = N signals at 180 and 183 p.p.m. None of these absorptions could be explained by (94) or (95). The ^1H .m.r. spectrum is also more suited to (96) than the N-arylindazoles as the low field aromatic doublet (τ 2.38, J 8Hz, 2H) is best explained by the protons H_A being deshielded by the C = N bond. The assignment of (96) to the thermolysis product of (93) is also in line with other reactions in this research and in the work of Jacquier,^{50,51} and Dürr.^{52,53,54}

CONCLUSION

The main object of the research (see Preamble), i.e. the determination of the factors influencing the modes of decomposition of diazoalkene



(1), was largely achieved. The importance of the proximity of the ends of the 6π -system, and the stabilities of the possible intermediates and products (diazoalkenes, carbenes, $3H$ -pyrazoles, etc.) is well established. The decomposition of such diazoalkenes appears, however, to have only limited value in the preparation of 1,2-benzodiazepines due to the competition of other reactions.

An unexpected development in the research was the van Alphen rearrangement of certain $3H$ -pyrazoles to give $4H$ -pyrazoles rather than the N -substituted isomers. At the time these rearrangements were carried out there was no literature precedent, but the results later gained support from the work of Jacquier^{50,51} and Dürr.^{52,53,54}

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